A TEXT-BOOK

OF

PATHOLOGICAL ANATOMY

AND

PATHOGENESIS

BY

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TRANSLATED AND EDITED FOR ENGLISH STUDENTS

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PREFACE TO PART I.

I HAVE first of all, at Professor Ziegler's request, to say something with regard to the German original of the text-book now offered to English students. His first design was to bring out a new and revised edition of Foerster's well-known manual of Pathological Anatomy. But as the revision went on, it became clear that the present state of our knowledge of Pathology could not be fitly represented without recasting and almost rewriting the whole work. It was, therefore, thought better that he should undertake an entirely new text-book, in which the subject should throughout be treated from a modern point of view. The great success of the first edition in Germany would seem to show that such a book was needed, and that the author's manner of treating the subject was approved by teachers of Pathology.

Professor Ziegler explains that a great part of his text is based upon observations made or verified by himself. Where he has drawn upon other sources he has carefully cited the needful authorities. "I am not blind to the fact," he adds, "that my statements and criticisms may bear too strongly the mark of my own personal views, and that these views may not be readily accepted by all pathologists. But I have, nevertheless, held it wiser not to introduce much matter of controversy into the text of a treatise intended mainly for students. Experience leads me to believe that the learner gains a readier and surer grasp of his subject when it is first presented to him as a uniform and coherent system of doctrine, even though the teacher's statement of it should border on the dogmatic. Once this grasp is gained it is easy for the more advanced student to master and

to appreciate other theories and doctrines. I have given in brackets full references to the literature of each subject discussed, and I have added such indications of its bearing as may prove useful to those who are engaged in pathological research."

The present English version was begun a year ago, on the basis of the first German edition. At that time there seemed to be no near prospect of a second German edition. In the first I found a considerable number of details which needed amendment or amplification in order to fit the book for the use of English students. The author very generously admitted my criticisms, and gave me full leave to make such changes as I might think useful. The work was well advanced, when a new edition of the first part was called for in Germany, and presently appeared. It embodied most of the improvements we had agreed upon, together with valuable additions. These I have now made full use of, so that this volume corresponds throughout to the second German edition. The matter in brackets has had my special care, and I have verified a very large number of the references. The original contains few allusions to English or French memoirs; I have therefore made it my duty to add full notices of such as throw light on the subjects treated in the text, choosing both original contributions and papers serving as a clue to previous work. This feature, and the careful revision of the main text, will, I trust, help to make the text-book useful to English workers in Pathology, even though they may be familiar with German.

The first part—on General Pathological Anatomy—is now published. It is practically complete in itself, and on some subjects, such as Malformations, Inflammation, Etiology of Tumors, and Bacteria, it gives a fuller account of modern teachings and discoveries than has yet appeared in any English manual. The second part—on Special Pathological Anatomy—is in course of publication in Germany. It is hoped that the English version of this part may be ready soon after the German edition is completed.

I owe more than I can well express to the kindness of Professor Klein; he has read through the proof-sheets of this volume, and has sent me many very useful suggestions and criticisms. Without his encouragement, and that of Professor Greenfield, I should not have ventured to undertake the work. I would also gratefully acknowledge the willing help I have received from my friends Professor Cossar

Ewart, Dr. J. F. Payne, and Dr. S. H. Vines; and from one whose loss I shall never cease to feel—Frank Maitland Balfour.

The beautiful drawing of tubercle-bacilli, somewhat inadequately represented by Fig. 80, was kindly sent me by Dr. Heneage Gibbes, of King's College, London.

In the multitude of references given I can hardly hope to have escaped all error. Any corrections or queries which may reach me shall therefore have my grateful attention.

DONALD MAC ALISTER.

ST. JOHN'S COLLEGE, CAMBRIDGE, ENGLAND,
December, 1882.

PREFACE TO PART II.

The very rapid sale of Professor Ziegler's text-book in Germany has led to an unforeseen delay in the completion of the Second Part. Two editions of the sections already published having been exhausted, the Professor has been obliged to give to the preparation of a third edition of these the time he hoped to spend in completing the remaining sections. My own purpose was that the second volume of this English version should conclude the book, but in view of the requests which reach me from every side I have thought it better to bring out the first eight sections as an instalment than to put off the publication of the whole for another year. The third and concluding volume is already in hand, and will be of about the same size as the present. It will contain the sections on the Kidney, the Lungs, and the Nervous System, together with general indexes to the whole work.

In the third German edition the arrangement of the articles has been recast, and other changes of form have been made but in order to preserve the continuity of the English version I shall follow throughout the plan of the first volume. This plan has been generally approved, and it appears to be the most convenient for English students.

My renewed acknowledgments are due, and are very heartily rendered, to Professor Klein and Professor Greenfield, who have read and commented on each sheet as it passed through the press. Dr. George Thin has in like manner done me the kindness of reading the chapters on the Skin. Professor Ziegler has given me his ready help on many

points, and has enabled me to utilize his additions to the text of the later sections. Dr. Sims Woodhead courteously placed at my disposal the drawing of *Actinomyces* from which Fig. 174 *B* was engraved.

In view of the generous aid I have thus received I am encouraged to hope that little in recent Pathology has been overlooked which is likely to be of value to English students.

DONALD MAC ALISTER

ST. JOHN'S COLLEGE, CAMBRIDGE,
February 1884.

PREFACE TO PART III.

When the second volume of this work appeared in 1884 I expressed the hope that the third and concluding volume would be ready in the following year. Owing in part to my increased academical duties, and in part to the unexpected demand for new editions of the volumes already published, I have been unable until now to find time for the fulfilment of my task. To the many readers in all parts of the world who have sent me friendly enquiries on the subject, I must here express my regret at the unforeseen delay. In some respects at least the work has not suffered thereby, for I have been enabled to profit in some measure by the valuable improvements which Professor Ziegler has made in the fourth German edition, and to bring up to date the references to some of the rapidly advancing parts of the subject. The indexes of authors and of subjects appended to the volume have been made with much care, and refer to the entire work.

It should be stated that the author, in order to give completeness to the text-book for German students, has with the help of his colleagues Dr. Haab and Dr. Wagenhäuser prepared an additional volume on the pathological anatomy of the Eye, Ear, Bones, Muscles, and Genital Organs—on what in fact is generally described as surgical pathology. After consultation with several teachers of experience I have decided to adhere to the plan indicated in the second volume, and

to leave these additional sections alone, at least for the present. They are not wholly Professor Ziegler's, and their subject-matter is perhaps more likely to be studied profitably in special text-books.

To the acknowledgments already made I have to add my sincere thanks to Dr. James Ross, who has read for me the pages on the Nervous System. His general approval of them gives me reason to hope that in this difficult part of the work I have not fallen into any serious error.

DONALD MAC ALISTER.

ST. JOHN'S COLLEGE, CAMBRIDGE,
October 1886.

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PATHOLOGICAL ANATOMY.

INTRODUCTION.

Life is known to us only in the concrete. It is indissolubly bound to a material substance. This substance, the basis of all the vital processes, is fashioned out of cells and their derivatives. All living organisms are made up of cells and cell-derivatives. The **cell** by itself appears originally as a microscopic mass of pale slimy finely granular matter, the so-called **protoplasm.** It usually contains within it a **nucleus**, that is to say a structure like a tiny vesicle, whose form may be round, oval, rod-like, or irregular, and in whose interior we can make out by proper handling, 1, small definite bodies, the **nucleus corpuscles**, 2, a net-like framework of **nucleus substance**, and 3, a clear fluid, the **nucleus juice.** The young cell is at first naked. Only in its maturer stages does it develop on its surface an optically distinct membrane or other structure according to the special tissue of which it forms a part.

The vital activity of the cell is of a threefold kind. It is directed in part toward its self-preservation, in part toward its propagation, and in part toward the ordering of its outward relations. Virchow distinguishes these severally as the nutritive, formative, and functional activities. Many of the functions of the cell (including the chemical changes which always accompany them) cannot be directly observed and are only to be made out by their effects. Others again, like motion, growth, and multiplication, can be observed in proper specimens under the microscope.

Every cell, whether it be isolated or joined with others, is influenced by the nature of its environment. This may work either to further or to hinder some or all of the functions of the cell. To a certain extent indeed the cell may exist unaffected by this influence in virtue of its own inherent properties, but the range of this independence is very limited. Let the external conditions deviate from the normal by more than a certain small amount and disturbances of the cell-functions at once show themselves. These disturbances may amount to the complete arrest of all signs of cell-life, or even to the utter destruction of the cell as such.

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An *Amœba* observed in a suitable liquid under the microscope manifests its vital activity by altering its form. It sends out fine prolongations from its pale finely granular body-protoplasm. It fixes one or other of these to some object in its neighborhood. Then its main mass flows toward them and blends with them again. If there be any fine particles suspended in the liquid and these happen to come within reach of the amœba as it moves forward, the animal flows round about them as it were, and so takes them up into its substance.

Let us now change the external conditions by raising the temperature a few degrees. The result is that the movements, hitherto perhaps slow and languid, at once become more lively—the vital activity of the cell is increased. Raise the temperature higher still—the movements gradually cease. At a certain degree of warmth the cell becomes quite stiff and still, and only when the temperature is allowed to sink to its former level do the original movements gradually reappear.

By cooling down the liquid we bring about a like result. The cell gradually ceases to move and becomes a mere inert globule. When the temperature is again raised it regains its power of movement.

Now add to the liquid a concentrated solution of common salt—the cell becomes turbid and shrivels up, its outline becoming irregular. Or pass a constant galvanic current through the liquid—the cell takes on a spherical form, becomes inflated, loses its fine granulation, becomes a mere vesicle with clear contents, and finally bursts.

These experiments show in clear and simple fashion how in consequence of changes in the external conditions the manifestations of life in the cell also change. The change may take the form of temporary increase, or of temporary diminution and arrest, or of permanent cessation. When the cell bursts we cannot pretend to doubt that it has ceased to exist as a cell ; it is in fact dead. Even the shrunken salted cell, though its structure may be less affected, must still be regarded as dead, for in no way can we succeed in again obtaining from it any manifestation of life.

Permanent cessation of all the functions of the cell is what we mean when we speak of its **death**; even though at first sight the anatomical structure of the cell is not destroyed.

But in the first experiments the case is very different. When the temperature is raised or lowered in a moderate degree, only one of the cell-functions is suspended, the function of movement. The nutritive activity persists ; hence it is that on readjustment of the temperature the motor activity is re-established. This cannot be spoken of as death. A condition in which there is not cessation of all the functions but only a partial suspension, diminution, increase, or alteration of any kind in some of them we distinguish as a morbid or diseased condition. The notion of **disease** is thus at the outset a physiological notion. We infer it primarily from the appearance of some abnormality among the accustomed manifestations of life. Disease is not an entity, capable of personification, of being placed in antithesis to health. The term **health**

merely denotes that the vital functions are being performed in a manner which experience has taught us to regard as normal. So by disease we merely imply a phase of life whose manifestations deviate in some way from the normal type.

Restoration of the functions to the normal type is **recovery**; cessation of all function is **death.**

The causes of the diminution and extinction of a cell's vital activity may be internal as well as external. No cell is endowed with the power of living on indefinitely. Certain cells or rather unicellular organisms, it is true, have the power of producing a long line of descendants merely by continual subdivision of their own substance, and in this way their vital activity appears to persist for an indefinite time. But life protracted after this fashion has also its limits. In the first place, it is unlikely that all the cells derived by subdivision from the mother-cell should receive at their birth exactly the same share of vital energy. Granting then that in the process of derivation an unequal transmission of the vital properties of the mother-cell to the daughter-cells is possible, we must also admit that the less favored descendants must sooner or later fail in their power to overcome the normal agencies antagonistic to cell-life. But even if this be denied, the life of the cell becomes at once finite so soon as we pass from the simplest unicellular organisms to higher multicellular forms. When division of labor is set up within the organism, and the production of new individuals is no longer a function shared in by all the parts of it, then it follows of necessity that some of the parts, some of the constituent cells, must be destined to perish.

How long a cell can live cannot in general be exactly determined. It depends on the properties transmitted to it from the mother-cell. We may say broadly that a cell's life is shorter in proportion as it stands higher in the scale of development, and as its properties are more specialized. Thus for example the ganglion-cells and gland-cells of one of the higher animals are always short-lived, and often fail to produce any progeny at all. On the other hand the number of cell-descendants of a vertebrate ovum, or of an amœba, is indefinitely large.

The death of a cell depending thus on internal causes is a physiological death. The gradual extinction of function which ushers it in does not fall within the category of disease : it is a phenomenom of age in the cell, a senile change, a senile retrogression.

Unlike this senile extinction of the vital processes a true disease is not a consequence of the indwelling and inherited properties of the cell. The efficient causes of a disease are always external. In the observations we made on the amœba it was heat or cold, an altered surrounding medium, or the galvanic current, which brought about disease and death. All these noxious influences are derived from without. And what we have here remarked in a single instance experience shows us to be universal. Autonomous as the cell may seem, it is yet unable, without external impulsion, to heighten its functions above the physiological

standard, or on the other hand to check or to suppress them. We can therefore give a still more exact definition of the notion of disease. By the term **disease** we are to understand **a deviation of some of the vital manifestations from the normal, the deviation being conditioned by external influences.**

But in considering disease as thus defined we must not limit our attention to the case of a single individual, or we shall find our dictum contradicted by everyday experience. If we could observe under the microscope the successive generations of a unicellular organism, and follow with certainty the life-history of each, we should come upon individuals whose functions were abnormally performed, and that although it might be impossible to detect any injurious external influence at work. We should then have to confess that the abnormal behavior was here, as in senile retrogression, conditioned by intrinsic properties. This would in fact be true, yet it would not contradict the above proposition—that disease can only arise through changes in the external conditions. If we had had before us a complete series of the cell's ancestors, and had noted all the phases of their lives, we should have found that the morbid phenomena of the last cell, though not immediately traceable to external influences, had yet already appeared in some of the foregoing generations. And there we should have found that external conditions existed which exercised a disturbing influence on the cell's life.

The morbid condition of the last cell then had not its origin in the cell's own lifetime. It was acquired from the mother-cell along with existence itself—the cell inherited it. We must thus distinguish **inherited** from **acquired** diseases.

What we have hitherto said of morbid life and death applies primarily to the individual cell. But the organism with which the physician and the surgeon have to deal is not unicellular. The human body is built up of millions of cells, and these cells differ one from the other in their morphological as well as in their physiological properties. Among unicellular organisms each single cell must exercise all the functions of life ; but in many-celled organisms the principle of the division of labor is carried to a high degree of completeness. Different cell-groups have built up organs differing utterly in form and substance ; even the component cells of the same organ are not all of the same nature. Notwithstanding this, we have no reason to suppose that what is true of the single cell is not also true of the various cell-groups.

The life of the entire organism as well as of the several organs is bound to the component cells ; it is the activities of the latter which we perceive and accept as the manifestation of life. As disease of the unicellular organism is but abnormal action of the single cell, so human disease is but abnormal action of a multiplicity of cells.

Naturally the question becomes now much more complex. With the multiplication of the cellular elements, with their differentiation into diverse organs, arises the possibility of local disease. Nay, it is all but

inconceivable that, when the complex human organism is invaded by disease, each and every cell should thereupon simultaneously err from its normal function. As a fact, experience shows that every disease has its local seat or seats; in other words it is not the entire organism which is diseased, but only some of its organs, or only individual cell-groups forming parts of organs. We speak therefore of **organic** and of **local** diseases. Which cell-groups become affected in any special case depends upon two factors: on the one side upon the external causes in operation, on the other upon the physiological nature of the tissue affected. A given injury does not affect every cell in the same degree. The vital properties of the cells of multicellular organisms are highly diverse, and so also is their power of resisting diverse influences. An injury that does not affect in the slightest the functions of one cell-group or organ may produce grave disturbances in those of another; a different injury may paralyze the tissues in one region, and in another stimulate them to increased activity. This difference in behavior can depend only upon causes inherent in the cell and arising from its specific properties. It is the evidence of a specific **predisposition** of individual tissues to specific disorders.

On the other hand the influences which can injuriously affect the organism as such are innumerable, and the manner as well as the seat of their operation exceedingly various.

If then we duly regard the great variety of the causes of disease on the one hand, and on the other the equally great diversity of structure and therefore of predisposition among the tissues, we shall not be likely to underestimate the difficulty that in most cases meets us when we try to determine the nature and the origin of a disease in man.

Here also it is true that the ultimate cause of disease is external; but the place and time and manner of its operation are far harder to determine than in the case of unicellular organisms. Sometimes it may be quite impossible to fix the ultimate determining factor, especially when an organ is attacked only in some of its elements and its functions are thus but slightly or imperceptibly affected.

There is still another fact to be considered—the **propagation** of disease from one organ to another. It often happens that an injurious agency which at first produces a morbid disturbance in one organ only, in its further progress invades another. This is brought about either by direct transition from one organ to its neighbor, or by actual transport of morbific matter through the blood-vessels and lymphatics to remoter regions. For example, a poison introduced into the intestine may be able to produce local disorder there; but if it be absorbed into the blood and so be carried to the various organs, it may further have the power of exciting grave functional disturbance in the brain; a different poison may leave the brain alone and influence the kidneys, and so on.

But this propagation of disturbance may take place in another way. Defective performance of its function by one organ is not always without

influence upon other organs. A morbid condition of one very often involves the like in another. Thus disease of the liver and bile-ducts may throw back the secreted bile into the blood, and this impure blood will tend to inhibit the action of the heart. Again disease of certain ganglion-cells in the spinal cord is followed inevitably by the atrophy of certain muscles. Failing action of the kidneys may bring on the general affection called uræmia. Imperfect action of the lungs may bring on serious changes in the action of the heart.

Next to external influences **heredity** plays an important part in the genesis of disease. Unfortunately its influence is not easy to estimate; and it is often difficult, often impossible, to distinguish the inherited from the acquired.

The human organism takes its rise in the maternal propagation-cell, the egg; and its development dates from the instant when in the act of impregnation the egg receives a specific stimulus from the paternal spermatozoa. The impulse thereby communicated manifests itself by cell-division and proliferation. According to the laws of heredity, the properties of the paternal and maternal organisms are transmitted to the child that is to be; and it is hence probable *à priori* that morbid conditions of the parents may be likewise transmissible to the child. This as a matter of fact is the case. The transmission shows itself in two ways. In the first place there are actual diseases, such as syphilis, which are bequeathed by the parent to the child. They are such that even in the womb or shortly after birth, or later still in life, they make their appearance in like fashion with the parental disease and without the intercurrence of fresh injury from without. Such are inherited diseases in the narrower sense of the term. They originate in a diseased condition of the ovum or spermatozoön which is transmitted to their cell-progeny, or in a direct transference of some morbific agent from the tissues of the father or mother into those of the newly generated organism. In the higher groups of animals the latter mode of transmission is the most likely one, and it has been actually demonstrated in certain special cases. They are not common.

More common than inheritance of a definite disease is inheritance of a morbid predisposition. By this is to be understood a certain debility of an organ or a tissue, not easy to define more exactly. This debility has arisen in the parents in consequence of some primary or inherited disease in them. In such cases an external cause is required to bring about the development of actual disease, and it is by no means necessary that the disease when it appears should be of exactly the parental type.

Inherited predisposition is oftenest observed in connection with nervous disease, and just in this region is best exemplified the fact that the type of disorder need not be the same in the child as in the parent. It is probable that the external or determining causes have an influence in this modification of type.

Distinct from inherited disorders are those which the fœtus acquires

within the maternal organism after conception. It is true that the fœtus is protected by the sheltering womb against manifold injuries to which in later life it becomes exposed. But it must not be forgotten that in this season of development, and especially in its earlier stages, its constitution is far frailer than in the mature condition. Nor must we leave out of account that its intimate relations with the maternal organism are in themselves a source of danger. Local changes in the uterus or in the fœtal membranes, and disorders of the mother generally, must obviously have an influence on the development and life of the fœtus. Experience proves indeed that the child *in utero* is subject to many and various diseases, and often enough perishes unborn. Certain diseases of the mother, such as small-pox, are directly transmissible to the fœtus. Others inevitably involve its death.

As above said, local changes in the uterus and in the fœtal membranes may also produce disturbances in the growing organism. To the investigator these do not show themselves primarily as disturbances of function; in the most favorable case he may perhaps be able to distinguish an abnormality in the movement of the heart or the action of a muscle. All that he finds on examination is the anatomical effect of the disturbance.

The fœtus is an organism whose function is to grow. If any one part of the developing organism meet with an injury, or if by any means a local disorder anywhere arise, the consequence is a local disturbance of the process of growth. If in other respects the fœtus develops normally and ultimately comes to be born, we shall find a corresponding abnormality in the conformation of the affected part. This may consist either in a defect, an overgrowth, an imperfect closure, or a misformation.

When the form or structure of a member deviates in this way from the normal, we describe it as a **congenital malformation**. It is the effect of a morbid process in the period of intra-uterine development, and may concern the whole or a part of the organism or of any one of its organs. Inasmuch as it is the effect of intra-uterine disturbance it is to be distinguished from acquired defect, mutilation, malformation, or overgrowth. The latter conditions arise in virtue of injuries sustained by the organism after it has become independent of the mother.

The question now arises, What are the special questions which fall to the lot of Pathological Anatomy in the investigation of morbid processes? Disease is nothing but a phase of life, in which one or more of the physiological processes is running an abnormal course. Is it then possible that the problems of life in disease can hopefully be attacked by anatomical methods? The observations that can be made during life upon diseased tissues—such as the skin, the epithelia, the eye—show that these methods are practicable; and the experience gained at the post-mortem table, from the microscope, or through actual experiment, confirms after death the conclusions drawn from the living subject. All these show that anatomical tissue-changes lie at the bottom of the morbid

phenomena observed during life; and that these tissue-changes are for the most part still recognizable after death. In other words they supply the justification for our previous postulate—that the diseases of man have always a local seat in some definite cell-group. Thus the primary and peculiar function of Pathological Anatomy is—to investigate, with all possible exactness and detail, the tissue-changes which are involved in the various forms of disease.

The information gathered in this field is already plenteous and important. Formerly diseases were of necessity classified symptomatologically; their names connoted certain groups of outward symptoms. Now, thanks to pathological anatomy, we are able to arrange them according to anatomical characteristics. We find this classification justified in practice by the constant recurrence of well-marked and specifically distinct anatomical changes in diseases whose whole course and character prove them to be in fact specifically distinct.

It cannot be gainsaid that as yet Pathological Anatomy has not succeeded in supplanting the clinical or symptomatic order of ideas. It is not yet possible in all cases to connect the morbid action of this or that organ with definite anatomical changes. We still must use the terms "epilepsy," "diabetes," to distinguish certain disorders; but that only implies that we are not yet able to replace the clinical conception by an anatomical one. It by no means implies that the several diseases are not dependent upon local changes in some special tissue or cell-group.

From the fact that we are sometimes unable to discover the seat of an affection we can only infer one of two things. Either the difficulties in the way of discovery are so great that we can only in certain favorable cases, not yet met with, succeed in overcoming them; or, that the tissue-change we are seeking eludes our optical appliances, inasmuch as it is not a change of gross structure, but one of chemical constitution and metabolism. This latter must at any rate be true of a vast number of trifling functional disturbances, whose transitory nature and slight intensity almost exclude the idea of a recognizable physical alteration of structure.

The various morbid tissue-changes which allow us in some measure to infer from the dead body the functional disorders experienced in life are either macroscopic or microscopic. A skilled eye can gather a great deal by mere inspection; and in this way a large number of diseases can be diagnosed on the post-mortem table. Still it very often happens that naked-eye inspection is insufficient, and it would in reality be much oftener so, if in previous similar cases the microscope had not already yielded us necessary information touching the minuter changes and the processes they involve.

Morbid changes have their seat in the cells, and in their derivatives the intercellular substances. It is therefore indispensable to a right understanding of these changes to call in the help of the microscope, and with it follow out the cellular and intercellular processes.

As a fact the microscope has in countless cases thrown an utterly unexpected light upon these processes, and the enormous advance of pathological anatomy in the last quarter of a century or so has been brought about simply by the exact attention bestowed upon them. Virchow it was who inaugurated this new method and established it on a firm basis. Microscopic examination of cellular and intercellular changes, in connection with naked-eye post-mortem examination, still remains the foundation on which our knowledge of disease and its nature must be based.

The amœba, which under changed conditions of life becomes languid and finally dies, undergoes before the last event certain visible changes. These enable the observer to follow the process of dissolution if not completely at least through all its more important stages. It is plain that a simple experiment of this kind, made on a single cell, can exhibit but a fraction of the normal and pathological processes that take place among the cells, cell-colonies, and cell-derivatives of complex organisms. The cellular processes which underlie the various diseases are extremely manifold and extremely diverse. He who tries for the first time to penetrate deeper into their nature, and to educe the significance of the changes he observes, will hardly be able to accomplish at once his designs and desires. He must first become familiar with the essential facts of the subject, which have been gathered and sifted out by the fundamental investigations of Virchow and the labors of Foerster, von Recklinghausen, Klebs, Cohnheim, Eberth, Rindfleisch, and many others.

The outcome of their labors is—that pathological processes fall into four great groups. If we follow the morbid processes in the order in which they attack the individual organism from its first beginning to its end, we naturally direct our attention first to those which affect its development.

The human being originates from a single cell by a process of continued cell-division. If for any reason a cell-group is not formed which naturally should be formed, the member or organ normally developed from this group will be lacking in the mature organism. A malformation is the consequence; and it is greater or less according to the number of cells undeveloped, and more or less obvious and striking according to the degree in which the symmetry and harmony of the whole is disturbed. When a structure is thus lacking or incomplete it is described as a **Hypoplasia** or **Aplasia**.

The second kind of morbid change ends also in defect of structure; not however through interference with growth, but through the destruction or degeneration of parts already formed. This may of course occur in the embryonic stage, and result in aplasia, or it may take place at a later stage as atrophy. These destructive or degenerative processes are not always alike; they may be rapid, or they may be slow and gradual; they may sometimes be extensive and obvious, sometimes strictly local and not at once perceptible. Changes of this kind are included under the term **Retrogression** or **Regression**.

In antithesis to these stand other processes distinguished as **Progression, Overgrowth,** or **Hyperplasia.** As the names indicate, the characteristic of these changes is an abnormally active growth, a too abundant cell-production. When they occur during embryonic life we have produced the so-called *Monstra per excessum ;* in other words we have structures excessive in relative size or duplicated. When they occur at a later stage, in the growing, stationary, or declining periods of life, they result in overgrowth of the organism as a whole, or of single organs or their parts, or lastly in so-called tumors. We may describe such changes as **constructive** or **formative.** Constructive and retrogressive disturbances of nutrition are not to be regarded as wholly without correlation. On the contrary, progressive processes not infrequently succeed to retrogressive ones, the object here being, if we may speak teleologically, to replace parts which have been lost. In this case the process is described as **Regeneration.**

A fourth type of morbid tissue-change is that known as **Metaplasia.** Metaplastic processes are such as lead to the transformation of one species of tissue into another. Sometimes they are retrogressive in character, sometimes rather constructive. The most important and most striking instances of this form of tissue-change are afforded by the cells. But the intercellular substances may also, and not infrequently, undergo more or less complete metamorphoses. Thus although we chiefly turn our attention to the cellular processes as after all the most essential, we must not altogether leave out of account the behavior of the intercellular substances. It is needful to note this, for the nature and condition of these substances have certainly some influence on the life of the cells themselves.

In each of these processes, retrogressive, constructive, and metaplastic, the condition of the circulatory system is of special importance. The regular and normal fulfilment of the function of circulation is essential to the maintenance of a tissue in its normal state. Disturbances of the circulation quickly bring about disturbances of function and changes in the tissues. Disturbances of the circulation play a distinct and highly important part in the process known as Inflammation. Unless we desire to limit this term to a single stage of the entire process, we may indeed say that the characteristic phenomena of Inflammation are those connected with the circulatory mechanism.

Pathological Anatomy has not fulfilled all its task when it has investigated the **morphology** of morbid change in cells and tissues. It must go on to determine the **genesis,** and the **causation** of morbid processes.

If we would obtain a satisfactory insight into the **significance** of the special changes that come before us, we must make it a first principle to compare these changes with each other, and with the known facts of physiology bearing on tissue-formation and degeneration. As our present ideas of the origin of specific forms of life only became possible after we had subjected animals to comparative examination and acquired an

exact knowledge of their embryology, so also must we study disease comparatively and investigate with exactness the processes of histogenesis, if we are to attain a satisfactory understanding of morbid phenomena. The appropriate objects for investigation will in the first instance consist of the morbidly altered tissues taken from the human subject ; but there will remain many questions for whose complete answer we must needs have recourse to experiments upon animals. The profound importance of these we may gather from the fact—that our knowledge of such diseases as can be artificially produced in animals is far more complete and thorough, than in the cases where the artificial methods have as yet failed us.

A knowledge of the **etiology** of the several forms of disease is of the very highest import. It is beyond dispute that a perfect understanding of the causes of disease and their mode of action is the end and goal of all research in morbid anatomy ; and it is the clear duty of pathologists to devote their energies to its attainment. If we could but define a disease, not according to its symptoms or its morbid anatomy, but strictly by referring it to its causes, we should gain far more than a clear comprehension of the affection ; we should have done much to settle the therapeutic treatment.

It has long been known that certain diseases arise in consequence of the settlement of certain plants and animals in the human organism. Only of late years have we learned that the domain of these parasitic disorders, as they are called, is of wide and far-reaching extent. Formerly we were acquainted with such vegetable and animal parasites only as are relatively large in size and easy to detect; in the last twenty years our improved optical instruments have made us aware of a great number of minute and hitherto unperceived species of parasitic organisms. The Schizomycetes, or *Bacteria*, especially have been recognized in recent years as the causes of certain most grave diseases. The observations now before us make it probable that the "bacterial" affections are very widely diffused. These investigations are of deep interest, and have vastly increased our store of facts concerning the diseases in question. It must not, however, be forgotten that the study of parasitic fungi can only make real and well-grounded additions to our knowledge of the associated diseases, can only in any measure yield us a true theory of them, can only lead us to a full understanding of the entire morbid process, when it has succeeded in making out the manner in which the fungi act, and the causal relation existing between fungus and disease.

Fungi have been detected in a large number of diseases, but only in a few cases have we gained an insight into their mode of affecting the organism. The mere presence of a fungus in the system cannot be described as disease. Disease only begins when, owing to the presence of the fungus, changes take place in the tissues of the organism which induce disturbances of their functions. Here then a wide field lies open to research. The detection of fungi in the diseased organism is but

the first step toward discovery of the cause of the disease and its mode of operation. It is a long way from this first step to the full and complete explanation of the entire process. This hiatus in our knowledge must not be too little thought of. The smallest contribution to the filling up of the gap is at least as welcome as the discovery of a new fungus—perhaps even more welcome. The pathologist must keep his attention well-fixed in this direction. Even though it may lie beyond his present powers to follow the processes in which morphological change is no longer detectible, and molecular transformation recognizable only by the chemist takes its place, there nevertheless remains a vast region still accessible to his means of research. In dealing with fungi we have to do with formed elements, with cells in fact. The changes they produce are changes in cells and their derivatives ; and in so much as relates to cellular processes and changes in formed protoplasm we have matter within the scope of anatomical investigation.

The path along which etiological research has to proceed is twofold —examination of the altered human organ on the one hand, experiment on the other. The former in this case cannot lead us to much. Experiment is by far the more promising way. If a given fungus disease can be produced in animals, it becomes at once possible to follow its spread and operation step by step ; we are limited only by our instruments and modes of examination. It is thus in our power, in comparatively short time, to acquire information which not even centuries of post-mortem investigation would suffice to educe. This method of research is confessedly of somewhat limited reach. To say nothing of the technical difficulties which meet the investigator, the number of microparasitic diseases capable of transmission from man to the lower animals is small ; or they run a course so different that their identity is not easily established. For such diseases therefore we are compelled to forego this valuable aid. If we will not decline the task altogether we must adopt another method; we must endeavor to make out experimentally the biological properties of the several fungi, as they are found in the human body. If we are successful, we have made it at least possible to form an idea of their mode of working upon the system. Of recent years both methods have led to brilliant results.

But there are sources of disease other than parasitic—such as high temperature, cold, chemically active substances, etc. These must not be overlooked. Though they are for the most part not themselves amenable to anatomical methods, their effects upon the tissues are.

Knowledge of the morphology, the genesis, the etiology of morbid changes is thus the aim and object of pathological anatomy. Its methods are post-mortem examination, direct or microscopic, on the one hand; experiment on the other.

On comparing the domain of the pathological anatomist with that of the clinical observer, it will not escape our notice that there is a gulf betwixt them. One has to do with death, the other with life ; one with

what has been, the other with what is and is to be. To bridge this gulf is the task of pathological physiology ; hers it is to bind into one the scattered facts which pathological anatomy has gleaned; to discover and make sure the link that connects the morbid change with the disordered function. Standing with firm foot on the ground of anatomical research, and leaning on experiment as her staff, it is her part to explain to the physician the phenomena he has observed at the bedside of his patient. She analyzes the complex of clinical phenomena into its elements, and from them reconstructs the natural types and species of disease. Through her mediation anatomical research joins hands again with practical medicine.

SECTION I.

MALFORMATIONS.

CHAPTER I.

GENERAL CONSIDERATIONS.

1. By **congenital malformation** we mean an anomaly in the form and make of the body as a whole, or of individual parts of it, referable to a disturbance of normal intra-uterine development. The degree of malformation may be very different in different cases. When the deviation from the normal is slight, affecting perhaps only a single part, we speak of it as a simple **anomaly**. The term malformation is not usually employed unless the misformed part or organ seriously disturbs the balance and harmony of the bodily form as a whole, seeming in fact to be ill-matched with the rest of the organization. When the deviations from the normal are very considerable the affected individuals are spoken of as **monsters.**

Monsters fall into two great groups—the single and the double. In **single monsters** we have malformation occurring in a single individual. One or more parts of the organism may have been arrested in growth, and are therefore incomplete or wanting; thus we have monsters by defect (*monstra per defectum*). Or the structure and disposition of the parts may deviate from the normal, and thus we get monsters by perversion (*monstra per fabricam alienam*).

Double monsters are of several kinds. Two nearly similar individuals may have one or more parts in common; or a properly formed individual may have attached to it the ill-developed body of a second as an appendage; or lastly particular members may be doubled, or simply exaggerated in size (*monstra per excessum*).

[The literature of malformation is rich both in comprehensive treatises and in accounts of individual cases. The following sketch is based on the works of Foerster ("Die Missbildungen des Menschen," Jena, 1865); Gurlt (Article "Monstrum" in the "Encyclopädisches Wörterbuch der medicinischen Wissenschaften," vol. xxiv., and "Virch. Arch.," vol lxxiv.); Ahlfeld ("Die Missbildungen des Menschen," Leipzig, 1880); and Perls ("Lehrbuch der allgemeinen Pathologie," Part ii., 1879). Foerster, Gurlt, and Ahlfeld give summaries of the ancient and modern literature of the subject. The student may also consult Vrolik's article on "Teratology" in "Todd's Cyclop. of Anatomy," and Lowne's "Catalogue of Teratological Specimens," Royal College Surgeons, London, 1872.]

2. The human organism is developed from the ovum. This is a cell of definite and regular structure, which is set into activity by the impulse of impregnation. The rudiments of the several parts are produced by continued segmentation of the primordial cell. The morphological form of the embryo begins very early to appear, and depends ultimately on certain regular evolutionary processes which the several rudimentary organs undergo. These processes are histologically recognizable as lateral or central proliferations of the cell-complex, and the resulting outgrowths forthwith become differentiated into specific forms. The factors determining the special direction development is to take do not, in the first instance at least, lie in the external relations of the ovum, in its environment. They are rather to be sought in the inherent and inherited properties of the segmentation-cells. But at the same time the external relations are not without influence on the subsequent course of development. If these are abnormal, the process of embryonic growth may be thereby altered, arrested, or perverted.

Theoretically speaking the origin of a malformation may be of either of two kinds. On the one hand, the primary rudiment (in other words, the ovum) may have inherited a tendency to abnormal growth; on the other, a normal embryo may in the course of development be affected by disturbing influences from without which check its progress toward the perfectly developed form. Experience indicates that both events occur.

The recurrence of hereditary malformations in a family (such as excess of fingers or toes) can only be explained by the supposition that the abnormal tendency exists from the first in the embryo, having been transmitted to it from one or other parent. On the other hand the absence of one or more limbs, deficiency of the cranium, etc., observed only in isolated cases, are to be accounted for in a satisfactory way only by assuming that external causes of injury have affected the growing fœtus.

[Disturbing influences acting on the otherwise normal embryo play a far more important part than heredity in the genesis of malformations. This might be inferred from the fact that the term malformation has come to connote exclusively gross and obvious anatomical relations. These gross anatomical anomalies arise generally from external causes. The pathological peculiarities transmitted congenitally from parent to child manifest themselves less in anomalies of external form that in deficient or perverted function of the tissues, or in morbid predispositions. Such anomalies are to be detected only by minute anatomical examination, or they are incapable of anatomical demonstration at all.]

3. **Monstrosities by defect,** as they occur in man, are of many kinds. Many of them affect most gravely the shape and fashion of the human form; others, of trifling character and affecting none but internal organs, can only be recognized by anatomical examination. The con-

figuration of the body is most prejudicially affected by defective closure, whether total or partial, of the larger body-cavities (pleural, peritoneal, or cerebro-spinal); or, on the other hand, by defective development of the extremities.

The causes of malformation in any given case can only be approximatively determined, or referred to this or that hypothetical injury; nevertheless we can generally indicate the direction in which the cause of the defect is to be sought.

Monstrosities by defect are commonly malformations by arrest; they owe their existence to a local hindrance to the development of a normally constituted embryo. It is but seldom, and then chiefly in cases where the entire body is affected (as in dwarfs), that we can attribute the effect to heredity; even of such cases the hereditary ones form by no means the majority.

The influences which check and hinder growth are to be sought in alteration, injury, or disease of the uterus, or in disease of the fœtus itself. To the first class belong defective development or disease of the membranes and placenta (uterine or fœtal), adhesion of the amnion to the fœtus, abnormally small quantity of *liquor amnii*, tumors of the uterus, concussions of the uterus with separation of the membranes, hemorrhages in the membranes or in their neighborhood, etc. As concerns the fœtus itself, its development may be disturbed by inflammatory affections which it acquires by transmission from the mother (small-pox, scarlatina, endocarditis), or by inherited disease such as syphilis. In the earlier stages of development abnormal twists or flexures of the embryo may be enough to cause very serious hindrances to growth.

The influences we have cited may act in various ways. Many arrest growth mechanically by simple pressure; others hinder the circulation so that the fœtus, or some of its parts, receive too scanty a supply of blood, and thus the growth is retarded. Other affections, such as the inflammations, actually destroy parts already formed and so render their further growth impossible. Not infrequently several factors may act at the same time, or the malformation of one organ, like the heart, may involve detriment to the proper development of the others.

The point of time at which the disturbing influence makes itself felt may of course vary greatly, and so by consequence will vary the intensity of its effect. The earlier the injury the greater is usually its effect. The loss of a few cells in the earlier stages of growth may involve the absence of an entire organ or limb; while later on, after the general form is nearly complete, the same loss might not be noticeable at all. Malformations, in the narrower sense of the term, originate for the most part in the first three months of fœtal life. By the end of that time the general form of the body and its members is well defined. Later disturbances give rise rather to changes that manifest themselves after birth as congenital disorders; they are therefore more fitly regarded as the anatomical basis of fœtal diseases than as true malformations.

[Geoffroy St. Hilaire ("Histoire générale et particulière des anomalies de l'organisation chez l'homme et les animaux," Paris, 1832–37) rejects altogether the doctrine of the primary perversion of the embryo (Haller and Winslow) and refers the malformations by arrest entirely to mechanical influences. Panum ("Untersuchungen über die Entstehung der Missbildungen," Berlin, 1860) on the whole agrees with him, although he grants the possibility of a primary perversion. He produced malformations in embryo chicks by varying the temperature of the incubator, and by varnishing the egg-shells. Dareste ("Recherches sur la production artificielle des monstruosités," Paris, 1877) made like experiments, and produced malformations by arrest by placing the eggs vertically, varnishing the shells, raising the temperature above 45° C., and by warming the eggs in an irregular manner. He has lately ("Comptes Rendus," 1882) shown that abnormalities may be produced by prolonging the interval between the laying and the incubation of the egg.

On the significance of adhesions of the amnion to the fœtus see Jensen, "Virch. Arch.," vol. xlii.; Fuerst, "Arch. für Gynäkologie," 1871; Perls, "Allg. Pathol.;" Dareste, "Comptes Rendus," 1882. If a malformation is to be produced, the original injury must of course not be too grave, otherwise the embryo would die outright. Above all things it is necessary that the apparatus of circulation should be maintained in working order. If the embryo dies, it is either expelled with its membranes from the uterus; or it is absorbed, in which case the membranes undergo further changes before they are finally expelled. A malformed fœtus then can never sink below a certain minimum of development without perishing prematurely; unless indeed it manages to prolong its existence by attaching itself as a kind of parasite to a second simultaneously developing fœtus. Compare Art. 13.]

4. The malformations of single individuals, which we with Foerster have distinguished as *monstra per fabricam alienam* or **monstrosities by perversion,** consist exclusively of abnormalities in the viscera of the thorax and abdomen. To this class belongs the *Situs transversus* or right-and-left reversal of the position of the thoracic or abdominal viscera, or both. In this case we usually find, in addition to the change of position, other changes in the forms and relations of the misplaced organs. Here also we include the various malformations (mostly by defect) of the heart and great vessels. Lastly, we must mention the numerous malformations of the genital apparatus, especially those distinguished as true and false hermaphroditism.

The genesis of these malformations is in general to be referred to the factors cited in Art. 3. They are for the most part to be reckoned among the malformations by arrest.[1]

[[1] For further details on this subject see the chapters relating thereto in the Special Pathological Anatomy.]

5. **Double monstrosities,** *monstra duplicia*, have the entire body, or a part of it, duplicated. The duplicated parts are sometimes equally well developed, sometimes unequally. In the latter case one part is stunted, and appears as a parasitic appendage to a well-formed individual. We thus distinguish between **equal** and **unequal** double monstrosities.

Older theories had it that double monsters arose through the adhesion of two originally distinct ova (Meckel, Gurlt, G. St. Hilaire). It was even assumed that the membranes of two separate ova might disappear at the point of contact, and then that the two fœtuses might become fused together, so to speak. This view is no longer upheld.

All double monsters originate from a single ovum and are fashioned on a single blastodermic vesicle.

According to Koelliker, the first rudiment of the embryo appears as a round opaque white spot on the wall of the blastodermic vesicle. This is the embryonic area (*area embryonalis*), formerly misnamed the germinal area. The embryonic area originates in a thickening of the epiblast (ektoderm), produced by a proliferation of the cells of this outer layer of the bilaminar blastodermic vesicle. The embryonic area next becomes pear-shaped. At the same time there appears at its posterior extremity a rounded thickening, which is continued into a somewhat conical prolongation. This thickening is the earliest rudiment of the primitive streak, in other words, it is the region of the epiblast or ektoderm from which the mesoblastic layer is to begin to grow. From the primitive streak the mesoblastic layer spreads between the epiblast and hypoblast till it extends over the whole of the embryonic area, and at length passes its boundaries. It thus forms a marginal zone, called the vascular area (*area vasculosa*), around the embryonic area. When the primitive streak has existed for some time, there appears in front of it the medullary groove. Thereupon the embryonic area becomes differentiated into a vertebral zone adjoining the medullary groove, and an outer lateral or parietal zone. The various parts and members of the embryo are produced by the progressive development of both zones.

The genesis of a double monster may be accounted for in various ways. In the first place it is conceivable that two embryonic areas may arise on the surface of a single blastodermic vesicle. These as they grow may come into contact, and fuse with each other to a greater or less extent. Another possibility is—that in the same embryonic area two primitive streaks may appear, and subsequently two medullary grooves; these may remain distinct, or may in part become blended. Thirdly, we may suppose the primitive streak to be single, while the medullary groove is developed in duplicate either throughout or in some part of it. Finally, it may happen that in certain cases the duplication occurs at a still later stage, affecting either single parts of the vertebral or parietal zones, or the rudiments of the several organs as they develop from these zones.

Each of these hypotheses assumes that at some time or other a

duplication occurs in parts which normally are developed as single. In the first, the date at which duplication appears is that at which the embryonic area is first formed. In the others, the duplication takes place within the embryonic area itself. In the first three cases, the duplication occurs in structures which are axial ; in the fourth, it may be limited to parts which are lateral.

We are compelled to accept the hypothesis that a duplication of some part or parts of the blastodermic vesicle or embryonic area can take place, if we are to account for the genesis of double monsters. The only question is—how far it is possible for a duplication which has already taken place to disappear again, owing to subsequent fusion. For example, it may be asked—whether from two originally distinct embryonic areas nothing but separate homologous twins can ever develop ; or whether the twin rudiments can unite again at some later stage. This question cannot as yet be definitely answered, so far at least as concerns embryos of the age at which the blastodermic layers have become completely differentiated. On the other hand, it may readily be believed that two embryonic areas which are actually in process of formation may encroach on each other and so unite. Here we have to do not with a fusion of two formed and separate structures, but merely with a grouping or arrangement of cells (due to identical processes) taking place round two centres close to each other, instead of round a single one. It is perhaps best, in dealing with the genesis of the double malformations, to avoid assuming the occurrence of secondary fusion or reunion of primarily distinct rudiments ; and to refer them all to incomplete cleavage or duplication. The ultimate causes of such cleavage are unknown to us ; it is likely that they are partly internal and partly external.

[The views of different authors on this subject (the genesis of double monstrosities) are very various. Some, like Foerster, Virchow, Oellacher, Ahlfeld, and Gerlach, pronounce for the theory of cleavage. Others, such as Schultze, Panum, and Marchand, think that rudiments already more or less completely distinct may reunite. According to Rauber, two or more primitive streaks may be formed on a single embryonic area ; and these may meet at some point in their length and there fuse together. This is the "Radial" theory. Marchand maintains that two rudimentary embryos are formed, and then unite. The duplication of the embryo is, he thinks, referable to causes anterior to the segmentation, inherent therefore in the ovum before impregnation, or involved in the process of impregnation itself. In support of this hypothesis he adduces some recent observations on invertebrates, which make it probable that the admission of two spermatozoa to the ovum may lead to the formation of two centres of segmentation. In other cases it is said that two blastodermic vesicles may be formed, and give rise to a double monstrosity. L. Gerlach lately attempted to produce double monsters experimentally. He varnished over a number of hen's eggs before incubation, leaving

nothing uncovered but a Y-shaped space over the region of the primitive streak. Out of a number of trials he obtained, on one occasion, a *duplicitas anterior* (Art. 14), in addition to various other malformations. He infers that in chicks at least it is possible to produce double monstrosities by artificial means.

See Foerster, "Die Missbildungen des Menschen," Jena, 1865 ; Panum, "Untersuchungen über Entstehung der Missbildungen," Berlin, 1860, and "Virch. Arch.," vol. lxxii. ; Dönitz, "Reichert's Archiv für Anat. u. Physiol.," 1866 ; Dittmer, "Reichert's Archiv," 1875 ; Ahlfeld, "Archiv für Gynäkol., vol. ix., and "Die Missbildungen des Menschen," Leipzig, 1880 ; Rauber, "Virch. Arch.," vol. lxxi. ; Marchand, "Realencyclopädie der gesammten Heilkunde," Art. "Missbildungen ;" L. Gerlach, "Sitzungsberichte d. phys. med. Soc. zu Erlangen," 1880 ; Cleland, *Journal of Anatomy*, 1874.]

CHAPTER II.

MALFORMATIONS BY ARREST IN SINGLE INDIVIDUALS.

a. Arrested Development of the Embryo as a Whole.

6. If the development of the embryo as a whole be interrupted, one of two results will follow. When the disturbance is grave the further development of the embryo is rendered impossible; it either ceases to live forthwith, or it dwindles away and ultimately perishes unborn. A slighter disturbance may not exclude a certain amount of development, and as a result there is born a fœtus whose general form is normal, though in size it is small and puny. A dead fœtus cannot remain for long unchanged; sooner or later it undergoes certain retrograde alterations. In most cases, fœtus and membranes are expelled from the womb, and this constitutes abortion. In other cases, that is to say, in the earlier stages of its development, the embryo may be absorbed and so disappear, the membranes undergoing a different fate. Most commonly they are expelled at once; but at times they remain and pass through further changes. In this latter way is generally formed the so-called **fleshy mole** (*mola carnosa;* otherwise clot- or blood-mole). This is a flesh-like mass consisting of membranes and altered blood-clots. The clots form the greater part of the mass; they are the result of hemorrhages from the maternal placenta, and are not infrequently the efficient cause of the death of the fœtus.

In other cases, the villi of the chorion undergo a peculiar degeneration, increase in size, and at length form a mass of club-shaped or spherical translucent cysts. These give the ovum at first sight the appearance of a bunch of grapes (whence the German name *Traubenmole*, or grape-mole). The manner in which cyst grows out of cyst, and the absence of stems uniting the pedicles, render this comparison somewhat inexact. In England this "cystic degeneration" of the membranes is often described as a **hydatidiform mole.**

A still rarer product of completely arrested development is the so-called **lithopædium.** The fœtus dries up into a kind of mummy, while its superficial parts and the tissues inclosing it become calcified. This effect is oftenest found when the situation of the ovum is abnormal.

The second result of a general arrest of growth is **dwarfing** of the

entire body (*Mikrosomia* or *Nanosomia*). Sometimes in dwarfs the proportion between the several parts is abnormal; for example, the head is often inordinately large.

b. Arrested Development of Parts of the Body.

7. Malformations depending on imperfect closure of the cerebro-spinal cavity.

(1) **Acrania** (*Hemicephalus*, *Cranioschisis*) is a frequent malformation; it consists in an entire absence of the bones and integuments forming the vault of the skull. In most cases the brain is also lacking (*Anencephalia*), and the base of the skull is covered with a vascular mass of connective tissue, enclosing a variable number of cyst-like structures. More rarely there is found a pocket-like fold of dura mater, containing some brain-detritus. The forehead being imperfectly formed the eyes project strongly, and give these monsters a toad-like appearance. The parietal bones are entirely absent. The tabular portions of the occipitals, temporals, and frontals, may be wanting in whole or in part. If the supra-occipital be also wanting, while the upper cervical vertebræ remain unclosed, the monstrosity is spoken of as *Cranio-rachischisis*. In such cases the upper part of the spinal cord is also wanting or rudimentary.

The production of Acrania is referred by G. St. Hilaire, Foerster, and Panum to the collection of fluid in the cerebral vesicles prior to the fourth month of gestation (*Hydrocephalus*). Dareste and Perls dispute this view, on the ground that in Acrania the base of the skull is generally convex toward the brain, and cannot have been subjected to pressure tending outward such as hydrocephalus would produce. They therefore regard the cause of Acrania to be some pressure exerted on the cranium from without. Perls maintains that this external pressure may be exerted by the head-fold of the amnion; this may, he thinks, be stretched too tightly over the cranial flexure, and so arrest the proper development of the cranial vault.

Quite recently Lebedeff has offered a new explanation of Anencephalia and Acrania. He thinks these are due to the production of an abnormally sharp cranial flexure in the embryo. This occurs when the cephalic extremity grows at an unusual rate in the longitudinal direction, or when the head-fold of the amnion is retarded in its development. In consequence of the sharp flexure the closure of the medullary plate to form the medullary canal is prevented; or else the medullary canal already formed is obliterated. This explains very easily the subsequent absence of the brain, and of its membranous and bony coverings. The cystic structures found upon the base of the skull Lebedeff believes to originate from the folds of the medullary plate, which sink into the substance of the mesoblast, and are then constricted off from the main mass.

(2) **Hernia Cerebri** and **Spina bifida** are terms used to describe minor deficiencies in the walls of the skull or of the vertebral column, through which the contents of their respective cavities protrude. In the case of the skull, a sacculation appears on the surface, which contains either fluid (*Meningocele*), or brain-substance (*Encephalocele*), or both (*Hydroencephalocele*). The fluid may lie either in the subarachnoid tissue, or in the dilated and sacculated ventricle; in the latter case it is enclosed on all sides by brain-substance (*Hydrocephalus externus* and *internus*).

Hernia cerebri is oftenest found in the occipital region, and at the root of the nose. The size of the sac, as also the size of the opening in the skull-wall, are very various.

The malformation known as *Spina bifida* is generally limited to the sacral and lumbar regions of the vertebral column. The herniated sac is covered by the integuments, and contains either fluid only (*Hydrorachis externa* or *Spinal meningocele*), or fluid with a thin layer of cord-substance (*Hydrorachis interna* or *Hydromyelocele*). In the latter case, the central canal is dilated by the fluid.[1]

(3) **Cyclopia** or **Synophthalmia** is a malformation in which the orbits form a single continuous cavity. This may be either very small, containing a mere rudiment of an eye or none at all, or larger in size and containing one eye or two lying close together. The nose is wanting, or represented by a snout-like projection just beneath the common orbit. When the brain is examined, we find instead of the cerebral hemispheres an undivided pointed vesicle running from behind forward ; the optic nerve is often either absent or single, and the olfactory nerve is likewise wanting. The other parts of the brain may also exhibit various malformations. The malformation as a whole depends on the defective development of the primary cerebral vesicle, in consequence of which the optic vesicles remain either unevolved or in close contact with each other (Perls). Dareste thinks the cause is arrested development of the head-fold of the amnion.

[References: Foerster, *loc. cit.;* Dareste, *loc. cit.;* Perls, "Allgemeine Pathologie," ii., 1879; Lebedeff, "Virch. Arch.," vol. lxxxvi.; Marchand, *loc. cit.;* Ackermann, "Die Schädeldifformität bei der Encephalocele congenita," Halle, 1882.]

8. Fissural malformations depending on imperfect union of the branchial arches.

(1) **Cleft palate** (*Cheilo-gnatho-palatoschisis*). In this deformity a fissure extends from the upper lip through the alveolar process of the superior maxilla, the superior maxilla itself, and the palate. The hard palate is cleft along its line of junction with the vomer; in the soft palate the

[1 An interesting series of cases of Spina bifida will befound described in the *Medical Times and Gazette*, 2, 1858.]

fissure passes along the middle line; in the alveolar process it goes between the exterior incisor and the canine tooth. If the fissure is bilateral, there appears a yawning aperture above the mouth, which is wider and deeper according to the stage at which the development of the vomer, intermaxilla, and lip was arrested.

Very often the fissure affects only the upper lip (*Labium leporinum*, **hare-lip**); less often the palate alone, or the palate and superior maxilla. The slightest degree of fissure is probably represented by a slight notch or scar in the upper lip, or in another direction by a bifurcation of the uvula. Even slight fissures of this kind may, however, be bilateral.

These varieties of fissure depend on an imperfect union of the superior maxillary and palatal processes of the first branchial arch with the nasal process of the frontal, the intermaxilla, and the vomer. This union should normally take place in the third month. In some cases the cause of the cleft has been found to be a morbid adhesion of the amnion to the face. The malformation may be hereditary.

(2) **Schistoprosopia** and **Aprosopia.** If the development of the first branchial arch, and of the nasal process of the frontal, be still more seriously interfered with, we have instead of the middle of the face a mere gaping cavity. Cleft-palate has become cleft-face. In extreme cases, eyes and nose being also absent, there may be no face at all.

(3) **Agnathia**, or absence of the inferior maxilla, is due to arrested development of the inferior maxillary process of the first branchial arch. In consequence of this deficiency the lower half of the face seems cut away, and the ears come almost into contact with each other (*Synotia*). In special instances the superior maxillary process is also rudimentary, and the malformation is accompanied by Cyclopia, with imperfect cerebral development.

(4) In consequence of the partial persistence of a branchial cleft, we sometimes meet with fissure of the neck, the so-called **Fistula colli congenita.** This oftenest takes the form of an opening a little above and external to the sterno-clavicular joint; more rarely the opening is in the middle line, or higher up in the neck. Generally there is but one opening; sometimes, however, there are two symmetrically placed. The fistular canal is for the most part narrow and lined with mucous membrane; it passes upward and inward, and as a rule ends cæcally; now and then it opens into the trachea or the pharynx.

Sometimes such fistulæ have dilatations, or these may take the form of closed cysts filled with fluid (*Hydrocele colli congenita*), or of cavities containing epidermoid cells and cellular detritus (*Atheromata*). Fistulæ and cysts of this kind are usually formed in the site of the third or fourth branchial cleft. Their hereditary character has been established in numerous instances.

[On cervical fistula see Heusinger, "Virch. Arch.," vols. xxix. and xxxiii., "Deutsche Zeitschrift für Thiermed.," ii., 1875; Rehn, "Virch.

Archiv," vol. lxii.; Neumann and Baumgarten, "Arch., für klin. Chirurgie," xx.; Virchow, "Virch. Arch.," vol. xxxv.; Schede, "Arch. für klin. Chirurgie," xiv.]

9. Fissural malformations depending on imperfect closure of the pleuro-peritoneal cavity.

The abdominal surface of the embryo, which is that directed toward the blastodermic vesicle, begins about the third or fourth week to close in by converging marginal growth. This at first takes place only from the anterior and posterior ends, but afterward at the lateral borders also. At the end of this stage the only communication between the intestinal cavity and the vitelline or umbilical vesicle is by means of the omphalomeseraïc or vitelline duct. In the sixth week the duct becomes obliterated, but it happens not infrequently that the part next to the intestine persists as **Meckel's diverticulum**; this takes the form of a cylindrical or club-shaped sacculation of the ileum.

Clefts of the **abdominal wall.** The complete closure of the body-cavity occurs in the eighth week, but this is liable to several forms of interruption. The slightest degree of abnormality is that in which a peritoneal protrusion, containing a coil of intestine, persists at the site of the umbilicus. This forms a hemispherical bulging, from the apex of which the umbilical cord arises (*Hernia funis*). This malformation is common; the sac is usually small; it is less usual for the hiatus in the abdominal wall to be considerable. Cases, however, occur in which a fissure extends for nearly the entire length of the anterior belly-wall (*Gastroschisis* or *Fissura abdominalis*); this may even extend to the thorax (*Thoraco-gastroschisis*). In the latter case the development of the *laminæ laterales* toward the umbilical vesicle must have been very early arrested. It is even possible for the funis to be absent altogether, and then the umbilical vessels pass direct to the placenta. Occasionally the fissure is altogether unclosed; in other instances a kind of hernial sac is formed by the peritoneum and the amnion stretched over it.

Now and then we find that the abdominal wall is duly closed in the neighborhood of the umbilicus, while a fissure persists either above it or below it. If below it, the fissure is usually associated with imperfect closure of the allantois and so of the urinary bladder. The internal mucous surface of the bladder in this case appears externally, and is pressed forward and everted by the intestines behind. The genital groove remains unclosed, and the external genitals are ill-developed. This is known as *Inversio*, *Ectopia*, or *Ecstrophia vesicæ*.

Clefts of the **thoracic wall.** If the fissure is small and merely affects the sternum, it is described as *Fissura sterni*; if it is wider, so that the heart is covered only by membrane and integument and protrudes, it is called *Ectopia cordis*.

The efficient causes of these imperfections of development are seldom demonstrable. It may be that they depend in part on morbid adhesions

of the borders of the *laminæ laterales* to the amnion. Very frequently they are found in individuals affected with malformations in other parts, such as the genitals or anus.

[See Buhl, "Klinik der Geburtskunde von Hecker und Buhl," 1861; Wedl, "Wiener med. Jahrbuch," 1863; Ahlfeld, "Arch. f. Gynäk.," v.; Perls, "Allg. Pathologie," ii., 1879. On intestinal diverticula see Lockwood, *British Medical Journal*, 1882; Roth, "Virch. Arch.," vol. lxxxvi.]

10. Aplasia of the extremities and of the hip- and shoulder-girdles.

Defects in the development **of the limbs** are by no means rare. Different classes are distinguished according to the degree of malformation.

(1) *Amelus.* Limbs entirely wanting or replaced by wart-like stumps. Trunk generally well-formed.

(2) *Peromelus.* All the limbs stunted.

(3) *Phocomelus.* Limbs consisting merely of hands and feet, sessile upon the shoulders and pelvis.

(4) *Micromelus* (*Microbrachius*, *Micropus*). Limbs regular in form, but abnormally small.

(5) *Abrachius* and *Apus.* Absence of upper limbs, while lower are well-formed; and *vice versâ.*

(6) *Perobrachius* and *Peropus.* Arms and thighs normal; forearms and hands, legs and feet malformed.

(7) *Monobrachius* and *Monopus.* Absence of a single upper or lower limb.

(8) *Sympus*, or Siren-monster. Lower limbs coalescent, being first rotated backward so that the external surfaces come into contact. The pelvis is usually malformed, as also the external genitals, bladder, urethra, and anus. Feet may be wholly absent or represented by single toes (*Sympus apus*); or there may be one (*S. monopus*) or both feet (*S. dipus*) at the end of the undivided extremity.

(9) *Achirus* and *Perochirus.* Absence or stunted growth of the entire hand or foot is seldom observed. More frequently we find absence of single fingers or toes (*Perodactylus*); or coalescence of two or more (*Syndactylus* or "webbing").

(10) Of the several bones those most commonly wanting are the radius, fibula, patella, clavicle, and scapula.

[See Foerster, *loc. cit.*; Gruber, "Ueber angeborne Defecte der Hand:" "Arch. f. Anat. u. Phys.," 1863; Voigt, "Ueber congenitalen Radiusdefect:" "Arch. d. Heilk.," 1863; Julliard, "Sympodia:" "Gaz. méd. de Paris," 1869. Many cases of malformation of the limbs have been attributable to constriction and even amputation by folds or bands of the fœtal membranes, or by loops of the umbilical cord. Compare Abelin and Blix, "Jahresber. der gesammt. Med.," 1863; Bambeke,

"Annal. de la Société de Méd. de Gand," 1861; Baker Brown, "Obstetrical Transactions," viii., 1867. Dareste explains the formation of the siren-monster by supposing that the tail-fold of the amnion has pressed too tightly on the caudal end of the embryo.]

c. *Malformations and Malpositions of the Organs.*

11. We have seen that the form of the body as a whole is liable to manifold irregularities, resulting from disturbances in its development. The several organs may likewise, and from like causes, deviate in form and structure from the normal. Especially is this the case with the genital organs and with the heart, which very often exhibit anomalies depending on arrested development. But malformations affecting the alimentary canal, the kidneys, the lungs, or the brain, are by no means rare. These will more naturally fall to be discussed in connection with the pathological anatomy of the respective organs.

Very frequently, too, we meet with **malposition** of the organs. This reaches its highest degree in the so-called *Situs transversus* (or *inversus*) *viscerum;* this is a right-and-left reversal of the viscera, the contents of the thorax and abdomen being transposed as if reflected in a mirror. It occurs in single as well as in double monsters.

But apart from the viscera, malpositions also occur in connection with the extremities. Under this head must specially be mentioned congenital dislocations, or displacements of the articular ends of bones from their sockets; and also abnormal positions of the feet, the hands being less often misplaced.

According to the position of the foot we distinguish four types:

(1) **Pes varus** (commonly though less strictly called *Talipes varus*), or club-foot. The inner border of the foot is directed upward, the outer downward; the heels inward; the astragalus projects strongly outward; the scaphoid bone lies beneath the inner malleolus. The calf-muscles and tendo-Achillis are shortened.

(2) **Pes valgus**, or flat-foot. The outer border of the foot is directed upward, the inner downward; the sole outward. The peronei and extensor muscles are shortened.

(3) **Pes equinus**, or (as we might call it) tip-foot. The heel is drawn upward; the tendo-Achillis shortened.

(4) **Talipes calcaneus**, or hook-foot. The toes are drawn up toward the front of the leg. The tibialis anticus, the peroneus longus and brevis, and the extensors, are shortened.

[References on *Situs transversus*:—K. E. Von Baer, "Entwickelungsgeschichte, i., p. 51; Valsuani, "Annali univ. di med.," February, 1869; Gruber, "Arch. f. Anat. u. Phys.," 1865; Buhl, "Mittheil. Münchner pathol. Inst.," 1878; Hickman, "Trans. Path. Soc.," 1869; Vallienne, "Étude sur les transpositions viscérales," Paris, 1881.

Transposition of the abdominal viscera alone is much more uncommon than complete transposition of all the viscera.

References on Congenital Dislocation: Hueter, "Gelenkkrankheiten," second edition; König, "Lehrb. der Chirurgie," ii.; Grawitz, "Virchow Archiv," vol. lxxiv.; Krönlein, "Deutsche Chirurgie," part 26, 1882.

The ordinary surgical text-books give details concerning the various congenital deformities of the hands and feet. On the genesis of club-foot see "Adams's Jacksonian Essay," London, 1873.]

CHAPTER III.

DOUBLE MONSTROSITIES AND MALFORMATIONS.

a. *Cleavage Affecting the Undifferentiated Embryo.*

a. Complete Cleavage of the Axial Structures.

12. Forms in which the development of the **segments** is **equal.**

(1) **Homologous twins;** these are produced when the development of the divided rudimental embryos goes on without check or hindrance. Homologous twins are always of the same sex. Each twin is enclosed in its own amnion, though portions of the membranes may disappear where the two are in contact. The placenta is almost always single and common.

(2) **Thoracopagi.** If the two rudimental embryos lie near or in contact with each other, a double monster may result. If portions of the trunk, that is of the thorax or abdomen, are coalescent, the monster is described as *Thoracopagus.* As the umbilicus and umbilical cord are single and common, the term *Omphalopagus* is sometimes applied to it. The various forms of this monstrosity are named from the extent to which coalescence is carried.

Xiphopagi are those in which the ensiform processes are united by a cartilaginous bridge. The peritoneum passes for some distance into the connecting structure (the well-known Siamese twins were xiphopagi).

Sternopagi are xiphopagi with a common thoracic cavity. The sternum may be double or single; the heart also double or single, in which latter case it is malformed; the alimentary canal is in part common; the liver double, though the two organs are connected by processes of gland-substance. Two of the upper limbs may be coalescent (*Thoracopagus tribrachius*), or two lower limbs and the pelves (*Th. tripus*). If the heads as well as the breasts and bellies have coalesced, we have a *Prosopo-thoracopagus*, *Cephalo-thoracopagus*, or *Syncephalus.* If a face be formed on the posterior aspect of the head as well as on the anterior, the monster is described as Janus-headed or *Janiceps.* Generally one of the faces is a mere rudiment (*Janiceps asymmetros*). The liver of the right-hand twin is usually "perverted" in position; more rarely this is the case with the other viscera also. Thoracopagi are the commonest kind of double monsters.

(3) **Craniopagus** is a pair of twins whose heads are adherent. They are distinguished as frontal, parietal, or occipital according to the locality of the adhesion. They are rare.

(4) **Ischiopagus** is a monstrosity in which the twins are united only at the pelvis. The spinal column and pelvis is duplicated, but the latter forms but a single wide girdle of bone, in which the two sacra are at opposite sides. This double pelvis carries two or four limbs. The trunks arise distinct and bent away from each other.

[In preparing this systematic survey of the double monstrosities use has been made chiefly of Ahlfeld's work, "Die Missbildungen des Menschen," Leipzig, 1880, and of the chapter in Perls's "Allgemeine Pathologie." Both treatises give references to the literature of the subject.

The genesis of all these double forms seems most easily explained by supposing that two embryonic areas are formed on the surface of a single blastodermic vesicle, and that these as they grow come into contact and coalesce at some part or other of their periphery.]

13. Forms in which the development of the **segments** is **unequal.** These forms fall into two groups. In the first, the nutrition of one twin is somehow cut off, and it dies without alteration of its external form. In the second group, the nutriment of one twin is derived from the other. As a result the form of the first or **parasitic twin** is more or less affected. The parasite may be more or less intimately incorporated with the "autosite" or host, as the fœtus is termed which finds nutriment both for itself and its neighbor. Or again, the parasite may be connected only with the placenta of the autosite. The following varieties have been distinguished.

(1) **Fœtus papyraceus.** If the umbilical vessels at their attachment to the common placenta come too close to each other, arterial anastomoses are formed between them ; the blood-current in one system may become more powerful than in the other, and thus the main stream is diverted toward the more powerful. The circulation in one of the fœtuses is checked, and that fœtus sooner or later perishes. The secretion of its liquor amnii ceases at the same time. The dead fœtus becomes more and more compressed by the growing one, and may ultimately become reduced to a thin flattened remnant. In other cases, the death of one of the fœtuses is determined by hemorrhage into the villi of the chorion, or by torsion, knotting, or compression of the umbilical cord.

(2) **Acardiacus.** This is a monster devoid of a heart ; it is always very imperfectly developed. The rudimentary fœtus is either free, and connected with the well-developed one only through the placenta ; or it is adherent to the well-developed one and blended with it to a greater or less extent (cf. *Teratoma*). In the first case the acardiac twin is in fact an allantoid or placental parasite ; its umbilical vessels are connected with those of its host, and its blood is kept in circulation by the host's

heart. According to Claudius, Foerster, Ahlfeld, and others, the monstrosity results from the later development of the allantois in one fœtus than in the other. The retarded allantois is prevented from reaching the chorion, and is compelled to insert itself into the expansion of the other allantois. The course of the circulation in the parasite being inverted, its heart is either wanting or rudimentary. The lungs, trachea, pericardium, diaphragm, sternum, vertebral bodies, and ribs, are absent or undeveloped ; as are also the liver and the upper limbs. The only organs which are fairly developed are, at most, those of the abdomen and pelvis. We frequently find in such cases an over-development of the subcutaneous connective tissue, giving rise to shapeless unorganized masses or tumors.

The different varieties of acardiac monsters are

(*a*) *Acardiacus amorphus.* This form is rare, and consists of a shapeless lump covered over with skin and containing mere rudiments of organs.

(*b*) *A. acormus.* Head developed ; thorax and abdomen absent or rudimentary. Very rare.

(*c*) *A. acephalus.* Head absent ; thorax rudimentary ; pelvis and attached members developed. This is the commonest variety.

(*d*) *A. anceps.* Trunk well developed ; head and limbs rudimentary ; heart also rudimentary. Rare.

(3) **Thoracopagus parasiticus.** Should one of the fœtuses of a thoracopagous monster be imperfectly developed, it will hang from the other in the form of a mere stunted appendage. The parasite is connected with the autosite by the ensiform cartilage, and the abdominal wall as far as the umbilicus ; it is therefore often spoken of as *Epigastrius.* It is seldom completely developed, *i.e.*, provided with all its members. In the majority of the cases on record, the parasite has been an *Acardiacus acephalus* or *acormus*, and its vascular system a mere outlying region or extension of the host's. This monstrosity is very rare.

(4) **Epignathus.** This is an amorphous acardiac monster connected with the mouth-cavity of the well-developed twin-fœtus. From this cavity protrudes a shapeless skin-covered mass, made up of cartilage, connective tissue, gland-tissue, brain-substance, teeth, bones, intestinal elements, muscles, skin, and fœtal down. In very rare instances the epignathus is attached to some other region, such as the orbit.

(5) **Teratoma.** Teratomata are tumor-like formations which are made up of a great variety of very different tissues, and so are distinguished from ordinary new-growths. Some of them contain rudimentary skeletal elements, such as those of the spine, pelvis, etc.; as well as rudiments of various organs, like the brain, intestine, different glands, kidneys, and muscles. Others contain tissue-formations of various kinds, such as muscular tissue, cartilage, skin, bony substance, gland-tissue, cysts, etc.; but no definitely formed masses which can be regarded as representing any special organ or member. The former tumors are un-

doubtedly to be viewed as remnants of parasitic fœtuses which have failed altogether to develop ; they are in fact *Acardiaci amorphi* in very close relation with the well-developed twin. With regard to the latter class of tumors, this view is not so certain. It is more likely that they depend in part for their origin on some disturbance or arrest of the development of a single fœtus, or on an aberration *in germine* (cf. Etiology of Tumors, Arts. 178, 179).

Regarded thus, the monstrosities *Epigastrius* and *Epignathus* become teratomata whenever the degree to which they are developed is less than a certain limit. Teratomata occur, however, most commonly in the form of large tumors attached to the extremity of the coccyx ; they are then spoken of as sacral teratomata, or teratoid sacral tumors. If the outward shape suggests that of a fœtus or a part of one, it is not hard to diagnose the case as an unequal form of double monstrosity. This is described as *Epipygus* (see Art. 14). When the tumor is of no definite shape, the diagnosis is not so obvious. In this case anatomical examination alone can settle the question, according to the principles just laid down. It is not to be forgotten, however, that new-born infants are liable to have tumors of the sacral region, which are not unlike teratomata, but which are really of the ordinary fibroid (or it may be the epithelial) kind.

(6) **Inclusio fœtalis.** In the form of fœtal parasitism just described, it usually happens that the parasite is more or less included and overgrown by some of the tissues of the autosite. This inclusion may be carried to a still greater extent. Teratoid tumors may be so completely enveloped by the body of their host, that they may be scarcely or not at all perceptible upon the exterior. This form of parasitism is spoken of *par excellence* as Inclusion. According to the region in which the teratoma is enclosed we distinguish the varieties :

(*a*) *Inclusio abdominalis* (or *Engastrius*).
(*b*) *Inclusio subcutanea.*
(*c*) *Inclusio mediastinalis.*
(*d*) *Inclusio cerebralis* (or *Teratoma glandulæ pinealis*).
(*e*) *Inclusio testiculi et ovarii.*

What has above been said of the teratomata applies also to these inclusions. In most cases so described, we have to do not with the enclosure of one fœtus by another, but with a pathological growth within the body of a single aberrant fœtus.

[Perls has brought together the literature of acardiac monstrosities in his "Allgemeine Pathologie," Part ii., p. 319. The above theory concerning their origin, put forward by Claudius ("Die Entwickelung der herzlosen Missgeburten," Kiel, 1859), and accepted by Foerster and Ahlfeld, is held by Perls to be inadequate. He thinks with Panum ("Virch. Arch.," vol. lxxii.) that one twin-fœtus may be seriously mutilated by constricting bands derived from the membranes, or by the funis ; that anastomoses may

be formed between its umbilical vessels and the placental circulation of the uninjured twin; and that thereupon the latter may, as it were, undertake the nutrition of the mutilated twin, which thus assumes the condition of a parasite. In support of this view he refers to an observation of Orth's ("Virch. Arch.," vol. liv.), who remarks that even a decapitated fœtus has in some such way continued to grow. See also Houston, *Dublin Medical Journal*, 1836.

Ahlfeld brings together the literature of *Epignathus* in the "Archiv für Gynäkologie," vii. Since then papers on the subject have been published by Sonnenburg ("Zeitschrift f. Chir.," v.); Verneuil ("Jahresb. der ges. Med.," 1875); Wasserthal ("Epignathus," Inaug. Diss., Dorpat, 1875); and others.

With respect to teratomata the following references may be given—Virchow, "Virch. Arch.," vol. liii. (Terat. of the Mediastinum); Arnold, "Virch. Arch.," vol. xliii. (Terat. of the Cranial Cavity); Weigert, "Virch Arch.," vol. lxv. (Terat. of the Pineal Gland); Braune, "Doppelbildung und angeborne Geschwülste der Kreuzbeingegend," 1862. With special reference to sacral teratomata see Depaul, "Jahresb. der ges. Med.," 1869; Reichel, "Virch. Arch.," vol. xlvi.; Lütkemüller "Oestreich med. Jahrb.," 1875; Böhm, "Berlin. klin. Woch.," 1872; Ahlfeld, "Arch. f. Gynäk.," viii., xii.]

β. Partial Cleavage of the Axial Structures.

14. **Duplicitas anterior.** The later the cleavage of the rudimental embryo is in appearing, the less extensive are its consequences. It may thus happen that part at least of the axis of the embryo remains undivided. Cleavages of the cephalic end (*Duplicitas anterior*) are the most common; those of the caudal end are rare. The slightest degree of anterior cleavage is indicated by duplication of the pituitary body. Next in degree come the clefts of the face (*Diprosopus*), of which there are numerous varieties gradually increasing in severity from mere duplication of the mouth-cavity to the formation of two distinct and complete faces (*Diprosopus distomus, diophthalmus, triophthalmus, tetrophthalmus, triotus, tetrotus*).

Dicephalus is a monstrosity consisting in duplication of the head and upper part of the vertebral column, and is either *dibrachius*, *tribrachius* or *tetrabrachius*. The latter form has two hearts and two pairs of lungs, and is capable of living.

Dicephalus parasiticus is very rare. The stunted fœtus has always a part of its vertebral column in common with the full-grown one.

The highest degree of anterior cleavage is called *Pygopagus*. The twins are then united solely by the sacrum and coccyx. The urinary and sexual organs may be either single or double. The equal form of this monstrosity is somewhat uncommon; the twins are capable of living.

The unequal form is more common, if we may regard as pygopagi some of the monsters described above (Art. 13) as epipygi and sacral teratomata.

[A pair of living pygopagous twins, born in South Carolina in 1851, has been exhibited as "the two-headed nightingale." An anatomical description will be found in the *British Medical Journal*, 1869, by Simpson, and in the "Berl. klin. Woch.," 1873, by Virchow. The cavities of the pelves were completely distinct, the sacral region alone being common.]

15. **Duplicitas posterior.** A monster in which the pelvis and lumbar portion of the spinal column are duplicated is described as *Dipygus.* The duplicated parts are very seldom equally developed; much more commonly one remains rudimentary (*Dipygus parasiticus*). In the slighter cases of this malformation, only individual parts of the pelvic bones or contents are duplicated. The lower extremities are duplicated, or there are but three of them (*Polymelia*). If the rudimentary pelvis is not visible externally, the supernumerary limb looks as if it sprang from a normal pelvis. It is usually very ill developed.

γ. Multiple Cleavage, and Overgrowth of the Entire Body.

16. **Homologous triplets** are produced when the rudimental embryo has undergone a complete threefold cleavage, and its subsequent development has been unchecked. They lie inside a single chorion, and the amnion may also be single; though cases occur where each fœtus has its own amnion. Frequently one or two of the triplets are malformed (*Acardiacus*). In consequence of a second partial cleavage in an embryo already completely divided, there may be formed a double monster together with a single ordinary fœtus—the whole being enclosed in a single chorion. This combination is not infrequent.

Tricephali, or three-headed monsters, arise from a second partial cleavage of an embryo already partially cleft; they are extremely rare. Of multiple cleavage occurring at both extremities of the embryo only a single instance is on record.

If the rudimentary embryo is of abnormal size, and undergoes no form of cleavage, the entire body becomes excessively developed. New-born infants weighing as much as ten kilogrammes (twenty-two pounds) have been met with. In other instances, the abnormally rapid or excessive growth has not begun until after birth.

b. Cleavage affecting the Rudiments of Particular Parts; Congenital Hypertrophy.

17. Cleavages affecting the rudiments of separate organs, and the multiplication of these organs or their elements which ensues, vary in significance according to their mode of origin. Some of them must be

regarded as conditioned by mechanical influences. Others are demonstrably due to heredity. Others still are referable to atavism, or the tendency of a higher type to revert to the organization of a lower.

(1) **Duplication in the limbs.** Cleavage of an entire limb, without duplication in the limb-girdle, has not been observed in the human species. Duplication of hands or feet is very rare. On the other hand, the duplication of fingers or toes (*polydactylism*) is a very common occurrence. The additional member is sometimes a mere appendage of skin ; in other cases it contains bones, and has the form of a perfect digit. The number of fingers on one hand may be as high as ten. Cleavage affecting the carpal or tarsal bones is rare.

(2) **Duplication of the mammary glands** (*Polymastia*). This occurs not very infrequently, and in men as well as women. The supernumerary mamma may lie close beside the normal one ; or it may be remote, having its seat on the abdomen, groin, or shoulder, at times even on the back. Double nipples are less often met with than supernumerary mammæ.

[See Leichtenstern ("Virch. Arch.," vol. lxxiii.), and Mitchell Bruce (*Journal of Anatomy*, 1879).]

(3) **Supernumerary bones and muscles.** These are very common. Extra vertebræ may occur in any region of the spinal column. Connected with the coccyx they may give rise to a tail-like appendage, though all so-called tails are not referable to multiplication of vertebræ.

Multiplication of the ribs (by the formation of cervical or lumbar ribs), and bifurcation of the ribs, are not infrequent.

Multiplication of the teeth is no rare occurrence.

[On supernumerary vertebræ and ribs see Welcker ("Arch. f. Anat.," 1881), Struthers (*Journal of Anatomy*, 1875), and Turner (*Journal of Anatomy*, 1870). On so-called tails see Ecker ("Arch. f. Anthrop.," xi.), and Leo Gerlach ("Morphol. Jahrb.," vi.).]

(4) **Duplication** (or multiplication) **of the** thoracic and abdominal **viscera.** This is commonest in the cases of the spleen, pancreas, ureter, and pelvis of the kidney. It is rare in the lungs, ovaries, liver, kidneys, testes, and bladder.

18. **Congenital hypertrophy,** or excessive growth of individual parts. Abnormal enlargement of one side only has more than once been observed. Excessive size of the head without hydrocephalus is rare, whether symmetrical or unilateral. Undue enlargement of one limb or part of a limb is more common. A hand or foot, a finger or toe, may thus grow to an excessive degree and so give rise to very serious deformity. The symptoms of excessive growth are generally apparent at birth. Sometimes the effect depends on a general hypertrophy of all the

elements of the member, sometimes on a mere over-development of adipose tissue.

Like the limbs, other organs also may reach abnormal dimensions by augmentation of their normal elements. This is the case with the thyroid gland, the tongue, the mammæ, the kidneys, the bladder, the uterus, the clitoris, the labia pudendi, and the penis.

[Full references to the literature of congenital hypertrophy are given in Kessler's "Inaugural-dissertation über einen Fall von Macropodia lipomatosa," Halle, 1869. Compare also Reid (*Monthly Journal Medical Science*, 1843); Curling ("Medico-Chirurgical Trans.," xxviii.); Trélat and Monod ("De l'hypertrophie unilatérale:" "Arch. gén. de méd.," 1869); Friedreich ("Congenital Unilateral Hypertrophy of the Head:" "Virch. Arch.," vol. xxviii.). Cases of congenital hypertrophy of the limbs are reported by Busch ("Arch. f. klin. Chir.," vii.); Freidberg ("Virch. Arch.," vol. xl.); Little ("Trans. Path. Soc.," 1866); Fischer ("Der Riesenwuchs:" "Deutsche Zeitsch. f. Chir.," 1880); Anderson (*St. Thomas's Hospital Reports*, London, 1882). A good instance of hereditary polydactylism is given by Lucas, *Guy's Hospital Reports*, London, 1881.]

SECTION II.

ANOMALIES IN THE DISTRIBUTION OF THE BLOOD AND OF THE LYMPH.

CHAPTER IV.

ANOMALIES IN THE DISTRIBUTION OF THE BLOOD WITHIN THE VESSELS—HYPERÆMIA AND ANÆMIA.

19. It is the office of the blood to convey nutriment to the organs and tissues. The cells and cellular structures, of which these are built up, cannot long continue to exist unless they are kept supplied with fresh nutriment. For this reason most tissues are furnished with blood-vessels, and those which are not so furnished are in intimate relation with others which are.

The demand for blood on the part of a tissue is not at all times equally great. Hence the supply may also undergo a corresponding increase or diminution, and with the incoming supply varies also the amount of blood actually present in the tissue. If a vascular organ happen thus to contain an unusually large amount of blood it is called **hyperæmic**; if it contains less than usual it is **anæmic**.

The regulation of the amount of blood, which an organ receives under physiological conditions, is effected by modifying the resistances offered by the arterial system. This modification of the resistances again is effected simply by means of changes in the calibre of the arteries. The quantity of blood contained in the entire body is insufficient to fill all the vessels at the same time. It is thus possible to increase the supply to any one organ only by diminishing the amount sent in other directions. The calibre of the arteries is altered by help of the elasticity of their walls and the contractility of their intrinsic non-striated muscles, and this apart from the action of changes in the blood-pressure otherwise conditioned. The intrinsic muscles of the arterial wall constitute the active regulating element. Their activity is dependent partly upon influences which directly affect them, and partly upon nervous impulses. These latter are transmitted to them from centres some of which are intravascular, and some situated in the medulla oblongata. They may act so as to contract the vessels, or to dilate them, as the case may be.

If the amount of blood in an organ deviates beyond the physiological limit from the mean or usual amount; or if there is a deviation dependent on factors other than the physiological ones; or if a deviation persists for an undue length of time, we have to do with a hyperæmia or anæmia which is pathological. Such pathological deviations are produced by

agencies only in part identical with those which regulate the normal blood-supply of the organ.

[In this book, which deals with pathology, we can only sketch in the broadest outline the general physiology of the circulation. For further details we refer the reader to the chapters on the subject in the classical work of Cohnheim ("Vorlesungen über allgemeine Pathologie," second edition, Berlin, 1882). Many of the physiological remarks in the text are derived from these chapters. A summary of the main facts will be found in Foster's "Text-book of Physiology."]

20. **Hyperæmia** of an organ shows itself to the eye as a more or less intense reddening and turgescence. The redness will be bright or dark (livid) according as the contained blood is rich or poor in oxygen. In organs which are themselves strongly colored, the redness may be more or less masked, and its exact tint modified.

The reddening and turgescence are produced simply by the dilatation of the blood-vessels of the part, and their repletion with blood.

Hyperæmia is not easily observed in the dead body; what is seen represents at best but partially the degree of hyperæmia which may have been present during life; and that only in some organs. At death the greater number of the vessels, and especially the arteries and capillaries, empty themselves of their contents. This is partly due to the contraction of their walls; partly to the *rigor mortis* of the tissues in which they have their course. The contraction of *rigor* presses out the blood contained in them much as the pressure of the finger makes a reddened hyperæmic spot become pale.

It may thus come to pass that a membrane, which during life was hyperæmic and red, may after death appear pale and colorless. Or the only reminder of the pre-existing hyperæmia may consist of engorged veins and venules, which, on mucous membranes at least, run in purple branching tree-like courses over the surface.

21. Hyperæmia may be either active (congestive) or passive (mechanical). The first form depends on increased flow of blood to the part, or **congestion**; the second on diminished flow from the part, producing **engorgement.**

Active hyperæmia is either **idiopathic** or **collateral.** The former is the more important, and depends on a relaxation of the muscular fibres of the arteries. This relaxation is brought about by paresis of the vaso motors; or by stimulation of the vaso-dilators; or it may be by direct weakening or paralysis of the muscular fibres themselves (such for example as is produced by heat, contusion, or atropia). Collateral hyperæmia is merely the consequence of diminished blood-supply to some other part. It ensues first in the immediate neighborhood of the anæmic part; but afterward the diverted blood may be conveyed to more remote organs, which happen to stand in need of it.

The causes of **passive hyperæmia** are of a different kind. The veins are normally devoid of tonus. The resistances offered to the venous blood-current are chiefly due to gravitation. They are chiefly overcome by means of the action of the muscles ; in part also by the aspiration toward the thorax which takes place during inspiration. When the muscles are inactive and the respiration feeble, these important forces are no longer available ; the blood then tends to stagnate in the veins, and collects especially in those parts which are most dependent. This condition is often misnamed hypostasis, or gravitative hyperæmia. Enfeebled action of the heart favors its appearance. Uncompensated valvular disease acts in the same way ; the blood is imperfectly propelled into the arteries, and so tends more and more to accumulate in the heart itself and in the venous system.

A further very common cause of passive hyperæmia is the interposition of abnormal resistances in the course of the venous current. Of this nature are obliteration of veins by compression, ligature, coagulation of the contained blood, or thickening of the walls. The forms of engorgement depending on narrowing or obliteration of veins are very various. Often they are scarcely or not at all perceptible, inasmuch as neighboring veins may dilate sufficiently to provide for the complete drainage of the part. This has, however, its limits. When, for example, in the arm the greater number of the great veins are occluded ; or when in the leg the femoral vein is stopped up at Poupart's ligament ; or again, when the main renal vein is obliterated, it becomes impossible for the blood to find adequate exit ; the current becomes slower and slower, and the blood goes on accumulating in the engorged region. When the process is directly observed in the expanded tongue of the frog, the red blood-cells are seen to become tightly packed together, and to fill completely the lumen of the dilated veins and capillaries. This appearance is due to the fact that, as a consequence of the engorgement, an increased quantity of liquid plasma transudes under pressure from the vessels.

In the systemic circulation the engorgement is confined to the veins and capillaries ; the arterial blood-pressure remains unaffected by it. In the pulmonary vessels, on the other hand, where there is no very marked tonus (Cohnheim), the engorgement is propagated through the arteries to the right heart, and there gives rise to increased blood-pressure.

Congested tissues are bright red in color, engorged tissues on the other hand are dark purple or livid ; though it must not be forgotten that if air be allowed access the livid color may speedily change to a brighter red.

[True hyperæmia must, of course, not be confounded with post-mortem staining of the tissues. The arteries after death squeeze out by the contraction of their walls the greater part of the blood they contain. This passes into the veins, and being affected by gravity, most readily into the parts that are lowest. Such a pseudo-hyperæmia is called a **hypostasis**.

Reddened patches on the skin due to such post-mortem movement of the blood are called **livores.** They appear three hours or more after death, and commonly upon the back and sides of the trunk and the posterior surfaces of the limbs and neck. If there be already an ante-mortem engorgement of these parts, it will appear more intensely after death.

In order to observe the process of the engorgement which ensues when the circulation is disturbed, we may conveniently make use of the tongue or the foot-web of a frog which has been curarized (Cohnheim, "Virch. Arch.," vol. xl.). The object must be spread out under the microscope on a proper holder. For example, the tongue may very simply be arranged by turning it out over a cork ring glued to the stage of the instrument, and stretching it with common pins stuck into the cork. When the circulation is normal the pulsating arterial stream, as well as the continuous venous stream, are seen to be bordered by a zone of plasma. If now engorgement be induced by ligature of the efferent vein of the tongue, the stream becomes slower—the zone of plasma in the veins disappears—and both veins and capillaries become tightly crammed and dilated with the red-blood cells as they accumulate. After a time the tongue begins to swell up, as it becomes infiltrated with the transuded liquid.

The frog's tongue and foot-web are also very well adapted for studying the changes of the circulation in congestive hyperæmia, and in anæmia.]

22. Pathological **anæmia** is dependent upon **oligæmia,** or upon **ischæmia.** In oligæmia there is a general deficiency of blood throughout the body; the anæmia of the several organs is due less to defective distribution by the vessels than to the inadequate quantity of blood they contain. Ischæmia, on the other hand, can give rise only to local anæmia; it always implies a diminution of the blood-supply to the affected part. Ischæmia may of course coexist with oligæmia.

Pathological diminution of the blood-supply to an organ is often due simply to an abnormal increase of the normal resistance offered by the arterial channels; in other words, to powerful contraction of the circular muscular fibres of the arteries. In other cases, the resistances are pathological in character: such are, for example, compression, diminution of the lumen owing to morbid changes in the vessel wall, deposits on the inner surface of the vessel, etc.

The result of diminishing the calibre of an artery is, in the first instance, to slow and to weaken the blood-current behind the constricted point. If the artery be completely occluded, the circulation behind the obstacle comes at once to a standstill. Yet the later consequences of such obstructions to the circulation are by no means always identical. Everything depends on the question whether the arteries behind the point of obstruction have anastomoses of fair size connecting them with other arteries; whether in fact a collateral circulation is possible. If it be possible, the disturbance of the circulation at first produced is quickly

compensated by an increased blood-supply through the collateral arteries. The compensation will be the more rapid and complete as the collaterals are larger and more dilatable.

The case is different, however, when the obstructed artery has no arterial anastomoses beyond the obstruction, when it is terminal, as it is called. The diminution of the current beyond the obstruction cannot be compensated for, and the affected region becomes in the first instance nearly or wholly deprived of blood. This state of things may alter after a time, however. When the movement and pressure of the blood beyond the obstruction have sunk to a minimum, the propelling forces become at length insufficient to maintain the flow. The specifically heavier red blood-cells become stationary, and accumulate in the capillaries and veins. In this way the anæmic region becomes again filled with blood, but with blood which is stagnating, not circulating. The same thing happens when a terminal artery is completely occluded. The blood from the anastomosing capillaries is slowly urged backward under slight pressure into the anæmic region. Finally, there may be a reflux from the veins themselves sufficient to give rise to an accumulation of blood in the vessels of the anæmic region. This reflux will occur when in the latter vessels the blood-pressure has sunk to zero, and the usual resistances to reversed flow in the veins (such as gravity, or the presence of valves) are not in action.

A further cause of anæmia in an organ may be the excessive determination of blood to other organs. The entire amount of blood available may thus be inadequate to supply the non-congested organs. This is described as **collateral anæmia.**

All anæmic tissues are pale. At the same time they are limp and non-turgescent, and any proper color which they may possess becomes well marked.

CHAPTER V.

ANOMALIES IN THE DISTRIBUTION OF THE LYMPH—ŒDEMA AND DROPSY.

23. The **lymph** which bathes the tissues is merely a transudation from the blood, mingled with the products of tissue-change. The transuded liquid is taken up by the lymphatics from the lymph-spaces of the tissues, and carried back into the venous system through the thoracic duct. Every change in the circulation, which determines an increased transudation of liquid from the blood, leads by consequence to an increased saturation of the tissues. This increased saturation is generally balanced by an increased discharge through the lymph-channels. But this compensating action has its limits. If the transudation from the blood-vessels still increases, there at last comes a time when the saturation of the tissues with liquid can no longer be kept down, and so it rises above the normal degree. The condition in which fluid collects in the substance of the tissues is called **œdema.** When the fluid collects in the greater cavities of the body we have **hydrops** or **dropsy**. The liquid transudation in œdema and dropsy has never the same composition as blood-plasma ; it is always markedly poorer in albumen.

Tissues which are the seat of œdema swell up ; but the degree of swelling depends in great measure upon the structure of the tissue. The skin and subcutaneous cellular tissue may, in virtue of their structure, undergo extreme distention ; an œdematous limb may thus become enormously swollen. It looks pale, is doughy to the touch, and "pits" on pressure with the finger. It is customary to describe œdema of the integumentary structures as **anasarca.** If an anasarcous part be cut into, the fibrous bundles of the tissue are seen to be separated from each other by clear liquid, which trickles away from the cut surfaces.

Other structures, like the kidney, are much less capable of containing large quantities of liquid than are the integuments. When an œdematous kidney, therefore, is cut into, very little liquid flows from it ; but the cut surface looks moist and glistening.

The lung can hold a very considerable quantity of liquid. Owing to its narrow accommodation in the thorax, it cannot of course become very greatly distended. But it has within it a multitude of air-cavities, and these fill with liquid when œdema invades it. From these the liquid,

generally frothy with air-bubbles, may be squeezed when the lung is cut.

The amount of blood contained in œdematous tissues is variable, and so therefore are their color and appearance.

Cavities which are the seat of a dropsical effusion contain a greater or less quantity of a clear, generally pale-yellowish, seldom quite colorless, liquid. It has an alkaline reaction, and at times curds of fibrin may be found in it (Art. 35).

Compressible organs situate in the dropsical cavity may be flattened, and the cavity itself enlarged.

If the effusion of liquid be general throughout the body we speak of it as **general dropsy**; if limited to the abdominal cavity it is called **ascites**.

24. Three varieties of œdema may be distinguished, according to their mode of origin: these are—the œdema of engorgement, inflammatory œdema, and hydræmic œdema.

The **œdema of engorgement**, as the name implies, depends upon a disturbance of the circulation. If from any cause the outflow of blood from the veins is hindered, the blood tends to accumulate in the capillaries and venules (Art. 21). If the degree of obstruction exceeds a certain limit, the plasma seeks a lateral exit and escapes from the vessels. The amount of liquid thus escaping is proportionate to the discrepancy existing between the inflow and the outflow.

The escaped liquid is always poor in albumen, poorer even than the normal lymph. It contains, however, a certain proportion of red blood-cells, depending on the intensity of the engorgement.

The immediate consequence of increased transudation is an increased flow through the lymphatics. Often enough this may be quite sufficient to convey away all the liquid which escapes. If it is insufficient the liquid collects in the tissues and the result is œdema or dropsy.

Obstruction to the outflow through the lymphatics does not usually bring about œdema; direct experiments have demonstrated this. In the first place, the lymphatics of most parts of the body possess ample anastomoses, so that it is not easy for a stagnation of the lymph to occur. Even when the thoracic duct is occluded collateral channels may be opened up and the circulation restored. Furthermore, when in a limb, for example, the whole of the lymphatic outlets have been closed, if no more than the normal amount of transudation from the blood-vessels goes on, no œdema is produced. The blood-vessels themselves have the power of taking up again the lymph they have produced. If the thoracic duct be completely occluded, and no collaterals are opened up, then œdema is the result; it takes the form of ascites. At the same time the larger lymphatics become greatly distended with accumulated lymph.

Though lymphatic engorgement alone is inadequate to produce œdema, it may possibly increase an œdema which has already been produced by increased transudation from the blood-vessels.

25. The quantity and the nature of the liquid which escapes from the capillaries and veins depend not only on the intravascular pressure and the resistances to the flow, but also to a great extent on the character and condition of the vessel-wall. Alterations in the amount of transudation may thus be referable, not to disturbance of the circulation, but to changes in the vessel-wall, and especially in their endothelial lining. The vessel-wall may in fact be made more permeable for the corpuscular as well as for the liquid constituents of the blood by various causes. One of these is long-standing engorgement, involving incomplete renewal of the blood-supply to the vessel. More serious causes of injury are persistent ischæmia, imperfect oxygenation, chemical changes in the blood, very high or very low temperatures, and traumatic lesions. What the exact injuries are which these bring about we are not as yet able to say ; but it may fairly be imagined that they amount to a loosening of the connections between the endothelial cells of the intima (Arts. 96–98). It is in virtue of such alterations in the vessels that inflammatory and hydræmic œdema are produced.

As regards **inflammatory œdema** no doubt can exist that it originates in some vascular change. It occurs as an independent affection, in the form of a more or less local and circumscribed swelling with dropsical effusion ; but it may also, as a secondary phenomenon, accompany other processes, like severe inflammation. In the latter case it is often characterized as collateral œdema. Inflammatory œdema is distinguished from the œdema of engorgement by the fact that in the former the exudation is very much richer in albumen and white blood-cells ; it is also common for coagulation to take place in the dropsical tissues.

Hydræmic or **cachectic œdema** is very near akin to inflammatory œdema. It was formerly believed that hydræmia, in which the blood is impoverished of its solid constituents, and hydræmic plethora, or over-dilution of the blood with water, might directly give rise to increased transudation from the vessels. It was conceived that the vessel-wall acted like other animal membranes, through which liquids poor in albumen filter more readily than liquids rich in albumen. This is incorrect. Cohnheim and his pupils have shown that the vessel-wall is not to be regarded as a dead membrane ; it is a living organ. When hydræmia is artificially produced it is not followed by œdema. Even hydræmic plethora produced by overfilling the vessels with diluted blood, though it does lead to increased transudation, does not do so till the dilution has been carried to an extreme degree. Even then the œdema does not make its appearance at the parts which are the usual seat of hydræmic œdema in man. We must therefore look for another explanation of the œdema of cachexia and of nephritis (in which disease the function of the kidneys is disturbed). According to Cohnheim, they owe their origin, as we have said, to a change in the vessel-wall. This change is due to the watery character of the blood, or to some deleterious substance circulating in it.

Hydræmic œdema, we say, is near akin to inflammatory œdema; but it is not identical with it. This appears from the fact already alluded to —that the liquid effused in the former is much poorer in albumen than that in the latter, and that it contains considerably fewer of the corpuscular elements.

[The doctrine of œdema in its present form is essentially due to the work of Cohnheim and his school. This is true as well of the theory of œdema from engorgement as of the theory of hydræmic and inflammatory œdema. It was he who made out the nature of the disturbances of the circulation involved in passive hyperæmia, as well as the conditions which govern the morbid alterations of the vessel-wall. (See Cohnheim's "Vorles. üb allg. Pathologie," second edition, 1882, and his "Untersuchungen über die embolischen Processe," Berlin, 1872.) The researches on the consequences of hydræmia and hydræmic plethora were carried out by him in collaboration with Lichtheim ("Virch. Arch.," vol. lxix.). Solutions of common salt were injected into the vascular system of dogs, but no œdema was produced by this dilution of the blood. When the blood-plasma is increased in amount, almost all the secretions (urine, saliva, bile, intestinal juice, etc.) are forthwith increased. The current of lymph in the lymphatics is also increased, but not in all parts; notably not in the limbs. In extreme hydræmic plethora the abdominal organs become œdematous, but never the limbs.

On inflammatory transudation and œdema, see also Lassar ("Virch. Arch.," vol. lxix.).]

CHAPTER VI.

ESCAPE OF THE BLOOD FROM THE VESSELS.—HEMORRHAGE. (THROMBOSIS, EMBOLISM, INFARCTION.)

26. **Hemorrhage** or **extravasation** implies an escape of blood (with all its constituent elements) out of the vessels into a tissue, or upon a free surface. It may be arterial, venous, capillary, or from all the vessels together, in which latter case it is termed "parenchymatous." Such an extravasation into a tissue takes on various appearances according to the quantity of blood which has escaped; and special names are given to some of these.

When the quantity is small and forms more or less sharply defined red or brown spots, these are called **petechiæ** or **ecchymoses**; when larger and less defined they are **sugillations** or **sanguineous suffusions.** If the affected tissue is completely infiltrated by the escaped blood, we speak of it as a **hemorrhagic infarct.** If the blood forms a tumor or swelling, it is called a **hæmatoma** or **blood-tumor.**

Hemorrhage in quantity always causes serious changes in the tissue invaded; not infrequently (as in the brain) the tissue is stretched, torn, and disintegrated.

If the bleeding take place from the free surface of an organ, the blood flows away either altogether or into the cavity which is bounded by the free surface.

Certain hemorrhages have received names from the localities in which they occur. Thus bleeding from the nasal mucous membrane constitutes **epistaxis**; vomiting of blood is **hæmatemesis**; bleeding from the lungs gives rise to **hæmoptoë** or **hæmoptysis**; from the uterus to **metrorrhagia**; from the urinary organs to **hæmaturia.**

A collection of blood in the uterus is called **hæmatometra,** in the pleural cavity **hæmothorax,** in the tunica vaginalis of the testicle **hæmatocele,** in the pericardium **hæmopericardium.**

Fresh effusions of blood have the color characteristic of arterial or of venous blood, as the case may be.

In the course of time the extravasation undergoes certain well-marked changes. Especially remarkable are the changes of color seen in ecchymoses and sugillations of the skin, which pass through tints of brown, blue, green, and yellow. Ultimately the extravasation is absorbed (Arts. 68 and 112–116).

27. The escape of blood from the vessels occurs in two distinct ways. A large and sudden hemorrhage always implies a solution of continuity in the vessel-wall. This has been distinguished as hemorrhage by **rupture** (*per rhexin, per diabrosin*) or, clinically, as apoplexy. Such solutions of continuity are the only causes of arterial bleeding; but from veins and capillaries bleeding may occur in another way, namely by what is called **diapedesis**. In this process the blood passes through a vessel-wall in which no rent exists. The escape is not sudden but gradual. The blood-cells slip through the vessel-wall one after the other. Liquid escapes at the same time; but it is not simply plasma, for it contains less albumen (Arts. 24, 25). These hemorrhages often remain small and circumscribed; but occasionally the process continues for a longer time, and then the infiltration of the tissue with blood-cells may go on to a serious extent. It must not be supposed that hemorrhage by apoplexy (or rupture) is always large, or hemorrhage by diapedesis always small. A rent in a capillary or a small vein will give rise to no great loss of blood; while the hemorrhage from long-continued diapedesis may reach an alarming magnitude. In a given case it is often by no means easy, often indeed quite impossible, to decide whether hemorrhage has occurred by rupture or by diapedesis.

[The process of diapedesis may be observed under the microscope. For this purpose the mesentery or the foot-web of a frog is used (Cohnheim). If the veins of outflow have first been ligatured, the capillaries and veins of the membrane are seen to be crammed with blood. After a certain time the red blood-corpuscles begin to escape from the capillaries and veins (compare Cohnheim, "Allgemeine Pathologie," i., and "Virch. Arch.," vol. xli.). The process is to be regarded as one of filtration (Hering, "Sitzungsberichte der Wiener Akademie," 57, 1868). As a result of the arrested outflow the blood seeks to escape laterally; it is in fact squeezed through the vessel-wall.

We owe to Arnold some very beautiful researches upon the diapedesis of red blood-corpuscles, as well as of other particulate substances introduced into the vessels ("Virchow's Archiv," vols. lviii., lxii., lxiv.). Arnold at first thought it must be admitted that at the points of escape of the particles holes or slits occur, which he called *stigmata* and *stomata*; afterward, however, he recognized the supposed openings to be merely aggregations of the intercellular or cementing substance of the endothelial cells. Under pathological conditions this substance becomes loose, and readily permits the corpuscular elements of the blood to pass through. Some beautiful physical experiments in illustration of the processes involved in diapedesis have been lately described by Hamilton ("Proc. Roy. Soc. Edin.," vol. xi.). See also Schklarewsky, "Pflüger's Arch.," vol. i.).]

28. The cause of rupture of the vessel-wall is either traumatic injury, or disease of the wall itself. In all so-called spontaneous hemorrhage we

must take it for granted that the latter cause is in action. Newly formed vessels are likewise very easily torn. Increased blood-pressure of course tends toward rupture of the vessel-wall, but it never actually produces it if the vessel be perfectly sound.

Diapedesis comes into play when the pressure is raised in the veins and capillaries, and also when, *cæteris paribus*, the vessel-wall becomes more permeable. It is very rapidly set up by obstructing the outflow of venous blood. The nature of the change in the vessel-wall which results in greater permeability is not yet completely understood; but it is known at least that the exciting cause of the change is a disturbance in tissue-nutrition (Art. 25). Thus it may be produced by temporarily checking the blood-supply of the vessel, or by direct injury to the vessel-wall. Moreover, certain poisons introduced into the blood may lead to the change. The vessel-wall must, in fact, be directly or indirectly damaged.

Sometimes the defective structure of the vessel-wall is congenital. There are persons who show a great tendency to bleed upon small occasion. These are called "**bleeders**," and are said to exhibit the **hemorrhagic diathesis** or **hæmophilia**.

What we may describe as an acquired hemorrhagic diathesis is exhibited in the diseases known as *morbus maculosus* or purpura, and scurvy; as well as in many of the infectious fevers and toxæmic affections, such as septicæmia, spotted typhus, small-pox, plague, *icterus gravis*, yellow fever, nephritis, phosphorus poisoning, etc. In some cases of *hæmophilia neonatorum* and of endocarditis, collections of bacteria have been found to be the originating cause of hemorrhage. Such hemorrhages are sometimes slight, sometimes very serious. They occur chiefly in the skin, mucous membranes, and serous membranes. Similar hemorrhages also occur sometimes in connection with troubles of the central nervous system, chiefly in the stomach and the lungs.

[Full references to the literature of hæmophilia are given by Legg, ("Hæmophilia," London, 1872, and *St. Bartholomew's Hospital Reports*, 1881), and by Immermann ("Ziemssen's Cyclop.," vol. xvii.).

Hemorrhages occurring in connection with brain affections have been observed in the human subject, and have also been experimentally produced in animals (Jehn, "Allg. Zeitschrift f. Psychiatrie," 1874; Charcot, "Leçons sur les maladies du système nerveux," i., 1875; Ebstein, "Arch. f. exper. Path.," ii.).

Ziegler has twice noted serious hemorrhages of this kind in epileptics. In one case three-fourths of each lung was completely filled with blood. He has likewise met with extensive hemorrhage into the lung in a patient who died of traumatic softening of the brain.]

29. The obstruction of arteries and veins plays the chief part in the production of irregularities in the circulation, and of hemorrhages. This

obstruction may arise in various ways, from without by ligature or compression, from within not infrequently by **thrombosis.** By this term is meant the formation of a coagulum or blood-clot within the vessel during life (Arts. 35 and 252–255). This coagulation occurs for the most part when the circulation is already weakened or arrested, and the vessel-walls diseased. The result is that the lumen of the vessel is first narrowed, and then as coagulation proceeds is blocked altogether. In the former stage the thrombosis is called **concentric** or **incomplete**; in the latter it is **obstructive.** Thrombi are formed oftenest in the veins, but they occur also in the arteries and in the heart. If a thrombus becomes loosened from the vessel-wall, and so gets into the blood, it is carried on by the current. In this way it may pass from the systemic veins into the pulmonary arteries, or from the heart and greater arteries into the smaller ones. It becomes then wedged in at the point where its size corresponds with the section of the vessel; and then by adapting its form to that of the lumen, or by setting up fresh coagulation on its own surface, it speedily blocks the vessel altogether. A thrombus thus swept into the vessel from a distance is called an **embolus.** It is generally situated at the bifurcation of an artery.

The consequences of embolism are very various. Often enough the tissue concerned is very slightly affected; in other cases it may undergo anæmic necrosis (Art. 33); in others still what is called embolic infarction.

30. The bleeding which sometimes ensues upon thrombosis of a vein is, as we have seen in Arts. 27 and 28, the immediate result of arrested outflow through the natural channels. The consequences of the closure of an artery have already been touched upon in Art. 22. The immediate consequences are these—First of all, the circulation is brought to a standstill, and the region beyond the block becomes anæmic. If the arterial twigs of this region are connected directly with some other unobstructed artery, the latter forthwith dilates and conveys a sufficient quantity of blood to irrigate the starved region. The circulation is thus speedily reestablished.

If, however, the vessels of the region possess no such collateral connections, the region itself is altogether deprived of fresh blood, and sooner or later perishes (Art. 33).

If the embolized artery be, as Cohnheim calls it, a terminal artery, having no arterial anastomoses, a scanty influx of blood to the tissues from the contiguous veins and capillaries may still be possible. It is in this way that a **hemorrhagic infarct** is produced. The capillaries of the anæmic region become gradually filled with blood, partly derived from the capillaries of neighboring regions, partly from slow reflux out of the veins. The blood oozing in from the neighboring capillaries is under a very low pressure. This pressure is insufficient to propel the blood out of the obstructed capillary system into the corresponding veins again. The blood therefore stagnates, and the capillaries become ever more and

more engorged. Of course, whatever reflux takes place from the veins can only carry blood into the capillary system; it cannot suffice to drive the blood through the capillaries.

In consequence of this engorgement, due to lack of propelling power, diapedesis is soon established, just as in complete obstructions of the venous outflow. The escape of blood is further aided by the disorganization of the vessel-wall, set up by the cessation or serious diminution of its supply of nutriment. The ultimate result of the diapedesis is the infiltration of the entire tissue with blood, and the formation of a firm, generally conical, hemorrhagic patch. Embolic infarcts of this kind are found chiefly in the lungs, the spleen, and the kidneys. As to their final fate see Art. 37.

[The fundamental experiments on thrombosis and embolism were originally made by Virchow ("Gesammelte Abhandlungen," Frankfurt a. M., 1856).

Virchow referred the production of the embolic infarct to increased flow in the arteries of the contiguous regions, consequent on the ischæmia of the region considered. This involved an increased lateral pressure within the vessels, and so increased tendency for the blood to escape. Cohnheim ("Untersuchungen über die embolischen Processe," Berlin, 1872), examining directly the results of embolism in the frog's tongue, established the existence of the reflux from the veins, the gradual refilling of the capillaries, and the escape of blood by diapedesis. The efficient cause of the diapedesis he considered to be an ischæmic disorganization of the vessel-wall. Litten ("Untersuchungen über den hämorrhagischen Infarct," Berlin, 1879) regards the reflux from the veins as non-essential, and refers the refilling of the capillaries to the influx from continuous regions. Even disorganization of the vessel-wall is, according to him, unessential to the production of an infarct; inasmuch as diapedesis is completely accounted for by the mere fact of engorgement (as is seen when the veins are obstructed). Diapedesis is for this reason increased when it chances that the blood coagulates in the vein of outflow from the embolized region.]

CHAPTER VII.

LYMPHORRHAGIA.

31. **Lymphorrhagia** occurs when a lymphatic vessel is ruptured and the contained lymph is effused into the tissues around. The pressure in the lymphatics is very low, scarcely higher, that is to say, than that in the contiguous tissues. An escape of lymph from the vessel can therefore occur only when a cavity already exists at the place of rupture, or when one is made by the same injury which rent the vessel. Thus in wounds, for example, we see lymph and blood escaping together; but the flow of the lymph can be arrested by interposing a very slight resistance. If the opening in the surface be not closed up after the rupture of a lymphatic, so that lymph continues constantly to escape, as sometimes happens in the case of ulcers, we have lymph-fistulæ formed. Such fistulæ may lead to the loss of very considerable quantities of lymph. The most important lesion of this kind, as well as the most likely to be dangerous, is **rupture of the thoracic duct.** This has occasionally been observed as a consequence of a wound; but more commonly of engorgement from closure of the lumen of the duct by inflammation or tumor. The lymph escaping into the thoracic or abdominal cavity gives rise to **chylous hydrothorax** or **chylous ascites.**

[References :—Curnow, "Lectures on the Lymphatic System," *Lancet*, 1, 1879; Day and Hill, "Trans. Clin. Soc.," 1869; Cayley, "Trans. Path. Soc.," 1866.]

SECTION III.

RETROGRESSIVE DISTURBANCES OF NUTRITION.

CHAPTER VIII.

NECROSIS.

32. Everything that lives comes sooner or later to an end—it dies. Death makes its appearance so soon as the vital energy of the organism, infused into it when it was first engendered, is exhausted in antagonizing external resistances.

Besides this death of the organism as a whole, or **somatic death,** we recognize what we must regard as a localized death; a death, that is to say, of individual cells or cell-groups, which we call **necrosis.**

The occurrence of local death or necrosis in a cell-group or entire organ is only in special cases associated with recognizable changes in structure. The slight histological changes the cells undergo in dying are not always enough to indicate with certainty the exact factor which has caused life to cease. The naked-eye appearances of the larger organs do not always betray the fact that some part of them has become necrosed.

Even the cessation of the obvious functions of an organ may leave us in doubt whether, as in necrosis, the cessation is permanent, or whether the functions are merely suppressed for a time.

Thus we can only subject necroses to anatomical examination, when death of the tissue involves change in its structure either consequent or antecedent. The latter occurs only to a limited extent; the former (*i.e.*, change consequent on necrosis) on the other hand is invariably found after a longer or shorter interval. The varieties of necrosis are in fact distinguished from each other according to the nature of these consecutive tissue-changes.

33. The injuries which lead to local death are divisible into three groups. The first includes those which destroy the tissue by their **mechanical** or **chemical** action. Thus external violence may crush a finger; sulphuric acid may destroy a patch of skin; and fungous parasites may disorganize the structure of a gland in which they are permitted to grow. A second group of injuries may be classed as **thermal.** If the temperature of a tissue be maintained at 54° C. to 58° C. for any time, the tissue is inevitably killed. Higher temperatures act still more rapidly. The lower limit within which life may be maintained is 16° C. to 18° C. A third cause of necrosis is **arrest of nutrition.** This produces "anæmic necrosis," and occurs very frequently in the human subject.

All causes which seriously interfere with the circulation of a part, and bring about permanent arrest of its movement, or **stasis**, may lead to the death of the affected tissue. Such causes are thrombosis, embolism, closure of the vessels by disease or ligature, pressure on the tissue, inflammation, hemorrhage, etc. The arrest of the circulation need not, however, be permanent ; it is enough if it persists longer than a certain time—necrosis still ensues. It is unimportant whether or not hemorrhage then takes place (Art. 30); this will only affect the external appearance of the part. Hemorrhagic infarction is thus pathologically equivalent to anæmic necrosis *plus* hemorrhage.

It is of course possible that mechanical, chemical, and thermal agencies may act together. Not infrequently they come into play successively in the same case.

The effect of a given injury in producing necrosis depends not merely on the normal character and strength of the tissue, but also to an essential extent upon its condition for the time being. A tissue whose nutrition has suffered in consequence of deficient or vitiated blood-supply, general marasmus, or hydræmia, is much more apt to necrose than when it is in its normal state. Thus in old patients, and in those suffering from uncompensated valvular disease of the heart, very slight injuries are enough to induce necrosis of the limbs. In emaciated typhoid patients the slightest pressure on the skin over the trochanter, elbow, sacrum, or heel, suffices to bring on gangrenous necrosis of the skin and subcutaneous tissues. Such necroses are described as senile or marasmic gangrene, and *decubitus* (bed-sores) or decubital necroses.

[The time required to produce necrosis by interruption of the blood-supply is different in different tissues. Brain tissue, renal epithelium, and intestinal epithelium, die within two hours (Cohnheim, "Allgem. Pathologie"). Skin, bone, and connective tissue, continue to live over twelve hours. In general it may be laid down—that tissues which exercise special functions die much more quickly than those which, like connective tissue, possess only the faculty of self-preservation, so to speak.]

34. The course of the necrosis (*i.e.*, the character of the tissue-changes it involves) is influenced by such circumstances as the nature of the tissue, its locality, and the form and cause of the necrosis. Not less important are the amount of blood and proper fluid or juice contained in the tissue, and the access or exclusion of air and of putrefactive ferments.

Moreover, there may be antecedent tissue-changes which are not without influence on the necrotic process, such, for example, as fatty degeneration, inflammation, and hemorrhage. We thus see that even if the necrotic process be in itself simple, *i.e.*, associated with only slight histological change, the consecutive changes it involves may yet be very manifold. We proceed to discuss the chief forms which have been observed.

A constant result of the death of a portion of a tissue is more or less

severe inflammation in the surrounding portions. This is most severe when decomposition sets in in the dead portion. By means of this inflammatory zone, the necrosed region is in a way marked off and isolated from the rest. The inflammation is hence described as **definitive,** and the zone as the **line of demarcation.** The process is more fully treated in Arts. 112–116.

Among the various terminations of necrosis we may distinguish four main types. We exclude special complications, such as the development in the necrosed tissue of specific irritant matters. In the first class, the dead tissue is absorbed and replaced by newly formed normal tissue (**regeneration,** Arts. 72–80). In the second, the dead tissue is likewise absorbed, but is not replaced by normal tissue; an inflammation *in situ* is followed by the formation of fibrous tissue, which fills up the gap in whole or in part (**healing by scar or cicatrix,** Arts. 112–116). In the third, the necrosed tissue is only partially absorbed, a part remaining as a caseous mass; this later on becomes in general calcified and enclosed in a capsule of connective tissue (**caseation** and **calcification,** Arts. 112–116). The fourth issue is the formation of a **cyst.** The dead tissue is absorbed, and in its place there is developed a small amount of fibrous tissue, but only over the boundary of the vacated space. In other cases, this space becomes filled with fluid, which is thus encysted. This happens oftenest in the brain.

a. Coagulative (Hyaline or Fibrinous) Necrosis.

35. Necrosis accompanied by coagulation occurs in two ways. In certain of the vital fluids like the blood and lymph, and in fluids which have escaped from the vessels, granular, fibrous, or homogeneous coagula are formed; that is one kind of necrosis. In the other, cells and cellular structures as they die become solid and firm, and coalesce into peculiar homogeneous or hyaline masses.

The granular, fibrous, and hyaline masses which make their appearance when blood coagulates are albuminoid bodies; and we speak of them in general terms as **fibrin.** This fibrin takes the form of flakes or curds, shreds, lumps, or membranes. If red blood-cells are enclosed in the meshes of the fibrin as it separates, the clots are soft and dark red in color. If coagulation does not take place in the plasma till this has separated from the red blood-cells, the clots produced are pale yellowish, soft, gelatinous, watery, translucent, and somewhat tenacious; after a time they contract and so become drier and tougher. In lymph, mere flakes only are formed. According to current theories, coagulation of the blood, or of the lymph, occurs when the white corpuscles die and dissolve in the plasma. Alex. Schmidt affirms that the plasma contains fibrinogen only. To bring about coagulation, that is the formation of fibrin, the presence of fibrinoplastin and of a ferment is necessary. Both of these are supplied by the white corpuscles as they dissolve in the plasma.

Inflammatory effusions or exudations may coagulate as blood does, and so yield masses containing a large amount of fibrin. These may lie on the surface of the inflamed tissue in the form of **false membranes** (Fig. 1). The fibrinous masses may be made up of granules, of delicate fibres, of coarse-meshed trabeculæ (Fig. 1, *c*), or of homogeneous flakes.

[Alexander Schmidt's researches on blood-coagulation are to be found in his paper :—"Die Lehre von den fermentativen Gerinnungen," Dorpat, 1876. Montegazza has pursued similar investigations—(Moleschott's "Untersuchungen zur Naturlehre," 1876). For other papers, see Gamgee's "Physiological Chemistry," vol. i., chap. 2. Wooldridge ("Proc. Roy. Soc.," 214, 1881, and "Du Bois-Reymond's Arch.," 1881) has recently published the results of a research conducted in Prof. Ludwig's laboratory at Leipzig, in which he seeks to make out that coagulation is mainly due to the action of deleterious liquids on the blood-cells. In

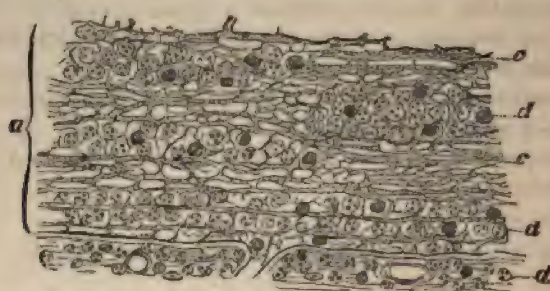

FIG. 1.—Croupous (false) Membrane from the Trachea. + 250. *a*, section through the false membrane; *b*, upper layer of the mucous membrane, infiltrated with pus-cells d_1; *c*, fibres and granules of fibrin; *d*, pus-cells.

shed blood the plasma "dies" and becomes deleterious in this sense; its action on the cells, especially the white cells, makes them break up and coalesce into a coagulum. A ten per cent. salt solution would have the same effect.

The factors of fibrin are said to be furnished by Hayem's hæmatoblasts, and by Bizzozero's "Blutplättchen." The latter have been recently described ("Centralb. f. d. med. Wiss.," 2, 1882) as small, very transient, delicate, colorless discs. According to Bizzozero it is the breaking up of his "Blutplättchen" which alone determines coagulation. The true significance of these bodies is not yet determined. They are perhaps mere decolorized red blood-cells.

Full discussions on the subject of fibrin and its origin are to be found in Virchow's "Gesammelte Abhandlungen," 1856. The intra-vascular coagulation of the blood is treated more adequately in Art. 252. It is possible that, in the coagulation of liquids contained in cellular tissues, the fibrinoplastic substance is yielded by the tissue-cells. These latter either dissolve altogether, or they permit their protoplasmic contents to escape in the shape of simple homogeneous masses.]

36. In the second form of necrosis with coagulation, the knowledge of which we owe chiefly to Weigert, the circumstances and the appearances presented are essentially different from those of the first. Here, as before, we have to do with the death of tissue occurring under special conditions, and resulting in the formation of coagulated albuminoids; but the coagulation takes place not in a liquid but in the substance of formed tissue-elements, in cells and cellular or intercellular structures.

If by reason of arrested nutrition, or by the action of chemical or thermal agencies, a definite segment of an organ be caused to die, and if then a moderate amount of lymph happen to flow through the necrosed segment, we have the conditions which give rise to coagulation within the tissue. The lymph contains fibrinogen, the cells contain fibrinoplastin; between them fibrin is produced. Cohnheim introduced the term **coagulative necrosis** to describe this special form of local death. Sometimes at least it may be fitly spoken of as hyaline necrosis. In this process the cells alter their appearance in various ways. The ultimate effect is always the destruction of the cells as such.

The varieties of morphological change observed in coagulating cells and tissues are dependent, partly on diversity of structure in the tissues, partly on the quantity of fibrinogen effused. The manner in which necrosis has been brought about is indifferent; but the dying of the tissue must not be too protracted, or degenerative processes, such as fatty change, may intervene and render the cells non-coagulable.

[The chief investigations on this subject of coagulative necrosis are those of Weigert. A summary of his results is given in "Virch. Arch.," vol. lxxix. The proof of the fact—that interfusion of lymph may cause the destruction of cells and the disappearance of their nuclei—was effected by introducing hardened pieces of tissue into the abdominal cavity of rabbits. These tissues were transformed in the manner described.

Similar cell-changes to those produced in coagulative necrosis, and more especially the disappearance of nuclei, may also result from mere putrefaction. Coagulative necrosis may also be found combined with other retrogressive changes, such as fatty degeneration.]

37. Among the numerous cases in which coagulative necrosis takes place must be mentioned **embolic infarction.** A certain time after the obstruction of an artery of the kidney or spleen, there is found lying beneath the capsule an opaque yellowish-white conical patch. This patch consists of necrosed kidney- or spleen-tissue, with perhaps fragments of disorganized and completely decolorized blood-clot. If the patch be microscopically examined in unstained sections, its structure will be found almost normal, though paler than the surrounding parts. The difference becomes, however, sharply defined when the section is stained, for the necrosed part is incapable of taking up color. The cells are strikingly pale and transparent, and their nuclei are either gone, or

swollen up and unstained. In later stages the outlines of t
come blurred, the nuclei vanish, and the cell-contents are met
into a finely granular fibrinous mass. Later still this mass d
and is absorbed (Art. 115). If the infarct was originally h
the effused blood, like the tissue-elements, is changed into
granular, or it may be homogeneous, mass.

[Minute investigations into the nature of hemorrhagic
have recently been made by Litten ("Untersuchungen übe
Infarct," Berlin, 1879) and Guillebeau ("Die Histologie d
farctes," In. Diss. Berne, 1880). According to Litten, renal
generally anæmic, *i.e.*, not accompanied by hemorrhage. Gu
the contrary, says that both renal and splenic infarcts ar
hemorrhagic, but become very quickly decolorized. Ziegler
the latter view, though he has examined recent infarcts in wh
unable to demonstrate either hemorrhage or its traces.]

38. The so-called **waxy degeneration of muscle** (Zen
an instance of coagulative necrosis. Muscle-fibre invariably
after death, but generally preserves its striation. Under va

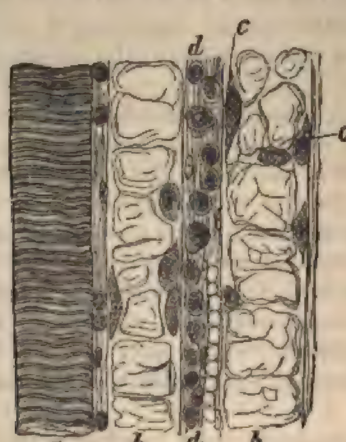

FIG. 2.—Waxy Degeneration of Muscle. × 250 (From a case of typhoid fever.) *a*,
fibre; *b*, degenerate muscle-fibre broken up into flaky lumps; *c*, regenerative cells lying
lemma; *d*, connective tissue infiltrated with cells.

ences, however, as *e.g.*, after bruising, forcible extension, rai
temperature, or febrile disease, the muscle substance is here
disintegrated, and the contractile myosin coagulates into
homogeneous mass (Fig. 2, *b*). This mass breaks up into sh
lumps. To the naked eye muscles so affected have a dull s
lustre, and look not unlike the muscles of fish.

Coagulative necrosis very often occurs in the course of in

processes. It is hardly ever quite absent where there has been copious exudation. In such cases it may take one of two forms. Either the effused fluid dissolves up the contained cells and then coagulates (Art. 35, Fig. 1, and Art. 102); or the tissue-cells themselves coagulate, forming homogeneous lumps or fibrous reticulated masses. To give an example, the ordinary stratified epithelial cells (Fig. 3, *a*) of the pharynx and soft palate in *diphtheritis faucium* (diphtheria) solidify into a peculiarly formed trabecular mesh-work (Fig. 3, *c*). Similar changes in the epithelium are observed in various cutaneous inflammations, such as small-pox. The ag-

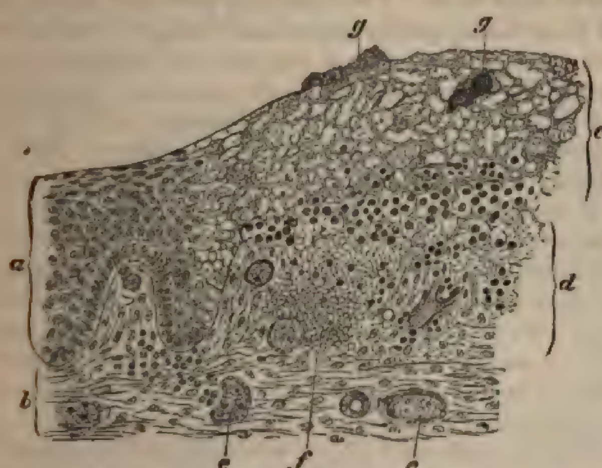

FIG. 3.—Section through the Uvula in Diphtheritis Faucium. × 75. (Aniline staining.) *a*, normal epithelium; *b*, normal areolar tissue; *c*, necrosed epithelium transformed into a coarse mesh-work; *d*, areolar tissue infiltrated with fibrin and leucocytes; *e*, blood-vessels; *f*, hemorrhage; *g*, heaps of micrococci.

gregations of cells which accumulate in simple inflammation may also solidify into pale hyaline flakes or granular masses. Such solidifications occur, for example, in typhoid infiltration of Peyer's patches and of the lymphatic glands, and in the cellular exudations which fill the pulmonary alveoli in caseous broncho-pneumonia. The formation of continuous hyaline masses out of cellular material may be typically seen in diphtheritic desquamation of mucous membranes (Arts. 103 and 425); the entire infiltrated tissue sometimes solidifies in this manner.

The ground-substance of connective tissue, hyaline membranes, the walls of blood-vessels, etc., are all liable to be transfused with coagulable liquid, and then to coagulate into homogeneous masses.

b. Caseation.

39. **Caseation** (or **tyrosis**) is a pathological transformation of tissue, whose product somewhat resembles in appearance firm new Cheshire cheese on the one hand, or soft cream cheese on the other. The name

refers merely to the outward appearance of the product; the process which leads to its formation is by no means always the same.

In the first form of caseation—in which the degenerated tissue is firm, tough, yellowish-white, and somewhat translucent—the process is one of coagulative necrosis. This occurs most frequently in tissues which are rich in cells; for example, in the foci of tuberculous disease, in cellular tumors, and in inflamed lung. A tissue which has become completely caseous is always devoid of nuclei, and is either homogeneous or finely granular. The transformation of a tissue into a firm cheesy mass may occur in one of three ways. The tissue may gradually assume as a whole a more and more homogeneous appearance, losing its nuclei the while. Or detached homogeneous masses may first be formed, which later on fuse together into a continuous mass. Or lastly, the tissue-cells may first dissolve and be replaced by granules and granular fibrils of fibrin; these last then close up and coalesce into a dense uniform mass. The last process is chiefly observed in the caseation of the cellular exudations of pneumonia; the first chiefly in tissues which, in consequence of chronic inflammation or tuberculosis, are the seat of a fibro-cellular hyperplasia. It should be noted that caseating masses originally homogeneous may, by subsequent transformation, take on a more granular appearance.

The softer form of caseation changes the tissue to a dull white. The chief part of the mass is made up of granular fatty and albuminous detritus. Neither cells nor cellular structures are any longer recognizable. This form of caseation is generally the result of a fatty disintegration of cellular tissues or exudations (Arts. 50–54), which have lost water by absorption. The tissue thereupon becomes inspissated, and its opaque appearance is due to the formation in it of minute oil-globules.

The firmer and softer forms of caseous change are not very sharply distinguished. At times both forms may be found together in one organ. It is even possible for the firmer form to be transformed, by processes physical or chemical, into the softer. The ultimate fate of caseous foci is either softening and liquefaction with absorption (Arts. 112–116), or calcification.

c. *Colliquative Necrosis or Softening.*

40. **Colliquative necrosis,** in which the affected tissue becomes as it were liquefied, is closely akin to coagulative necrosis. In each case the necrosed parts become saturated with liquid. Colliquation may thus either precede or follow upon coagulation. For example, the coagulation of the blood and formation of a clot is preceded by the liquefaction or solution of certain cells contained in the blood. A similar process may be observed in the case of blisters following upon burns.

The first change perceived is an enormous swelling up of the epidermal cells overlying the papillæ (Fig. 4, *d*); the cells being wholly or in part killed by the action of the heat. This swelling up depends on the ab-

sorption by the dead cells of the liquid which transudes from the papillary vessels. It becomes at length so extreme that the cell-substance dissolves completely and the cell-membrane itself disappears. Not until the tumefaction and colliquation have reached a certain point—*i.e.*, when the cell is distended to a mere vesicle, or has gone altogether—do the granular fibrils which indicate coagulation begin to appear (*f*, *g*, *h*).

In some tissues this coagulation after colliquation does not occur. Thus in **anæmic necrosis (softening)** of the brain we have simply disintegration and liquefaction of the brain-substance. The several constituents of the tissue break up, and dissolve in the liquid which is poured out from the vessels. They are then absorbed, and the liquid

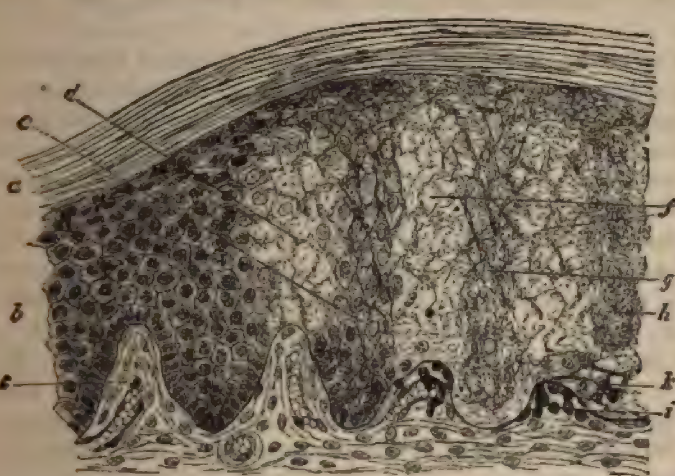

FIG. 4.—Section through the Epidermis and Papillæ after a Burn. × 250. The preparation (carmine-stained) is from a cat's paw which had been burned with melted sealing wax. *a*, horny layer; *b*, rete Malpighii; *c*, normal papilla; *d*, swollen epithelial cells (in some the nucleus is still visible, in others not); *e*, interpapillary cells (those below are uninjured, those near the surface are swollen and stretched); *f*, fibrinous mesh-work (composed of cells and exudation; cell-structure altogether lost); *g*, swollen cells without nuclei; *h*, interpapillary layer of cells stripped off and destroyed; *k*, subepithelial exudation (coagulated); *i*, depressed papilla, infiltrated with cells and disappearing.

becomes gradually clear again; but there is no coagulation. The reason of this probably is—that brain-substance contains but few coagulable matters, and on the other hand that the effused lymph, not being the result of acute inflammation, contains but little fibrinogen or fibrinoplastin. The same thing is at times to be observed in other tissues, as for instance in so-called "softening of the heart," when the muscle-substance has already undergone fatty degeneration. Here the antecedent degeneration has notably diminished the amount of coagulable matter in the muscular tissue.

But colliquation of the tissues may follow upon coagulation as well as precede it. It is a very frequent occurrence for coagulated exudations (as in croupous pneumonia) or thrombi to break down and liquefy. This liquefaction of coagulated masses is always accompanied by certain

chemical changes, the efficient causes of which are frequently of the nature of organized ferments (Art. 42).

d. Dry Gangrene or Mummification.

41. **Dry gangrene** is commonly the result of necrosis in parts which are exposed to the air.

Typical examples are afforded by the so-called senile gangrene of the extremities, especially of the toes and feet; and likewise by the necroses of the same parts following upon frost-bite. In the first case, the necrosis is determined by defective blood-supply, partly owing to general feebleness of the circulation, and partly to local changes in the blood-vessels.

The affected part is generally engorged with blood when necrosis sets in, and thus exhibits a dark or livid coloration. The engorgement is due to stagnation of the blood-current from mere feebleness of propulsion. After the death of the part, the coloring-matter of the blood transudes and gives the tissues their dark-red appearance. At the same time the tissues begin to dry up by evaporation. This drying process is notably accelerated when the epidermis separates, as happens when the engorgement has been extreme, and in frost-bite. The part becomes first leathery, and then perfectly hard, brittle, and black. Under the microscope the tissue-elements are seen to be shrunken and withered.

Dry gangrene or withering is a physiological process as it affects the stump of the umbilical cord in infants. Between the sound tissue and the gangrenous there is formed an inflammatory line of demarcation (Art. 115). Dry gangrene may at times occur as a later stage of moist gangrene.

e. Moist Gangrene or Sphacelus.

42. **Moist gangrene** is necrosis followed by decomposition and putrefaction of the necrosed tissue. If septic organisms reach a dead tissue which is rich in blood or other liquid, it very soon begins to decompose. The organisms may reach the part either directly from the air (as in gangrene of the skin or lungs), or through the channel of the circulation (as in gangrene of the testis, or of the foot). Parts which are exposed and abound in blood-vessels, such as the foot, become livid from diffusion of the coloring-matter of the blood. The epidermis frequently rises in blisters and bullæ. Soon the putrefying tissue begins to stink, and then to disintegrate. Slight mechanical causes readily give rise to wounds, and in these the tissue is seen to be infiltrated with discolored blood, and it is brittle or even tinder-like. Corresponding to the obvious naked-eye disintegration of the structure are the profound chemical changes which take place (Arts. 191, 192); and the final result is the total destruction of the tissue as such. Not infrequently gases are

evolved during the process, giving rise to so-called **gangrenous emphysema** (*gangrène gazeuse*). The rapidity of the destructive process depends greatly on the nature of the affected tissue. Bone preserves its form for a long time in the midst of a gangrenous mass, while the soft parts perish very quickly.

The microscope shows that in this process of decay septic organisms are always present (Arts. 192 *et seq.*). Blood-corpuscles quickly cease to be distinguishable, inasmuch as they break up and dissolve, or here and there become transformed into granular pigmented masses. Other cells become turbid, lose their nuclei, break up, and disappear. Fat-cells disintegrate, and the oil they contain mingles in small globules with the gangrenous mass. The fibres of the connective tissue swell up, grow turbid and ill-defined, and finally dissolve. Elastic tissue, tendon, and cartilage hold out for a long time, but ultimately perish in like manner. In general terms we may put it—that gangrene involves the gradual solution of the solid constituents of the tissue, and results in the formation of a dirty gray, grayish-black, or grayish-yellow, opaque, semi-fluid mass, mixed with shreds and remnants of various structures. The various normal elements of the tissue thus disappear in succession ; while new crystalline products of chemical decomposition appear instead, such as fatty needles of margarin, needles of tyrosin, spherules of leucin, "sarcophagus-crystals" of triple phosphates, and granules of black or brown pigment.

In the later stages of putrefaction, mould-fungi at times make their appearance on parts exposed to the air (Art. 221).

[Further details of the tissue-changes in gangrene may be found in Demme, "Ueber die Veränderungen der Gewebe bei Brand," Frankfort, 1857 ; and in Rindfleisch, "Pathological Histology" (Sydenham Society). See also Chauveau, "Nécrobiose et gangrène," Paris, 1873 ; Paget, "Surgical Pathology."

Putrid decomposition, and therefore also gangrene, can arise only through the agency of micro-organisms. Furthermore, the presence of a certain proportion of water in the tissue is essential. If the tissue dry up, the development of septic organisms ceases, or is at least seriously retarded ; and with it also the process of decomposition. The chemical products of the gangrenous decomposition of the tissues are hydrocarbons, ammonium sulphide, sulphuretted hydrogen, valerianic acid, butyric acid, etc. ; and ultimately carbonic acid, ammonia, and water.]

CHAPTER IX.

SIMPLE ATROPHY AND PIGMENTARY DEGENERATION.

43. In treating of malformations, we showed that in consequence of arrested development members, organs, or parts of organs may be ill-grown, misformed, or altogether wanting. Or if the plastic energy that determines growth be deficient, the entire organism or some of its parts may be dwarfed and stunted. Defective development of this kind, *i.e.*, aplasia or hypoplasia, may occur after birth as well as before it. So long as the organism continues to grow, so long as new parts or organs continue to be formed in it, so long is its growth liable to be checked by external or internal influences.

We may often observe this hypoplasia in the child. At birth it may have been anything but puny, yet under the operation of external causes, such as defective nutrition, various kinds of disease, or others less easily recognized, it later on shows signs of imperfect development in some of its systems or organs. The consequence is a dwarfing of the entire frame or of its parts, very often associated with faulty structure and function of the viscera. This hypoplasia makes itself especially evident when the bones are badly developed, as also when the heart and great vessels, the genital organs, or the central nervous system are undergrown. The association referred to is observed, for example, in cretins, whose bones are generally ill-grown; and in chlorotic females, where with hypoplasia of the vascular system there is also some imperfection of the generative functions.

Now **atrophy** is not to be confounded with such hypoplasias or aplasias. In atrophy we have to do not with defective development, but with retrogressive change in parts originally well formed and well grown.

44. The life of an organ, like that of an individual, is limited in its duration. The active cell-growth of the period of development is succeeded by a stage in which the formative activity is less marked. In the latter stage the equilibrium between cell-growth and cell-decay is maintained with but slight oscillations to one side or the other.

In old age this equilibrium is disturbed, and decay has the upper hand. An involution (the reverse of evolution) of the entire organism and of its parts takes place. Thus a man ultimately dies, even when there is no question of disease, so soon as the advancing involution of his

vital organs reaches a stage at which they can no longer efficiently perform their functions.

But besides this general retrogression, or senile decay, there is a physiological retrogression of particular organs, which takes place much earlier in life. The generative organs in woman lose their functional power long before extreme old age. The thymus gland has undergone complete degeneration by the age of adolescence. Various tissues, like the hyaline cartilage which is the first rudiment of bone, are in their very nature temporary structures. The several tissues then, like the organism itself, inherit but a measured lease of life.

Considered anatomically, retrogression shows itself in an organ by diminution of its size; microscopically, by diminution and ultimate disappearance of its constituent elements, especially of the elements which are special to it.

45. An organ, toward the close of its life, undergoes what we have called a physiological retrogression. But analogous retrogressive processes may occur, as it were prematurely, under pathological conditions. Their result we describe as **simple atrophy**.

This pathological atrophy is distinguished, like the other, by shrinking of the organ affected, or by diminution in size and number of its essential elements.

In the case of dense parenchymatous organs like the liver, kidney, heart, or brain, the shrinking is the first thing which is likely to strike us. If the shrinking has been uniform the surface remains smooth; if it has been irregular the surface looks uneven and granular, and the external form of the organ may be altered. On the other hand, atrophy of bone shows itself rather by thinning of the trabeculæ and widening of the medullary cavities, than by any general diminution in size. So too in the lungs, we recognize the occurrence of atrophy by the increased size of the air-spaces, and the loss in part of the alveolar septa.

Compared with the shrinking and loss of substance, the **pigmentary change** so often associated with atrophy is of minor importance. It is a secondary, non-essential phenomenon in the process. It depends either on the fact that the normal pigmentation of the tissue becomes more pronounced as the essential elements disappear; or on an actual deposition of pigment associated with the atrophic process; or lastly on some alteration in the amount of blood contained in the tissue.

46. The shrinking of an atrophied organ is due to the fact that its elements dwindle and disappear. Here, as in the case of senile involution, it is the proper and specific elements of the organ which suffer the most; and the supporting framework of connective tissue the least. It is in fact very frequently observed that the connective structures remain perfectly intact or even increase and grow, while the specific elements have already disappeared. Thus in the illustration (Fig. 5) of a muscle undergoing atrophy, the contractile substance (*a*) contained within the sarcolemma has distinctly dwindled (*b*). But the connective tissue sepa-

rating the fibrillæ remains undiminished; the nuclei of its cells seem even to have multiplied.

Similar appearances are readily observed in atrophied liver-tissue. There every one of the gland-cells may have vanished, and yet there may be no diminution in the amount of the connective-tissue framework. So

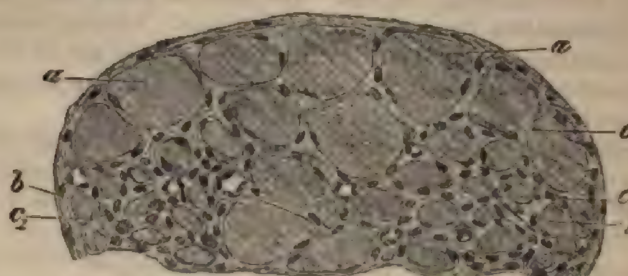

FIG. 5.—Section of an Atrophied Muscle. × 300. (From a case of progressive muscular atrophy: Bismarck-brown staining.) *a*, normal muscle-fibre; *b*, atrophied muscle-fibre; *c*, *perimysium internum*, in which the nuclei as at c_1 are seen to be increased in number.

too in preparations of brain and spinal cord, the ganglion cells may have altogether disappeared, without any visible change in the neuroglia.

[Adipose tissue is peculiar in its mode of atrophy. The fat in the cells breaks up into small oil-globules which are absorbed; the empty cells return to their first condition of ordinary connective-tissue cells. At times the disappearance of the contained fat is followed by proliferation of the nuclei (**atrophic proliferation**). If serum transude into the tissue after the fat has gone, the tissue becomes gelatinous in appearance (**serous atrophy**). If, lastly, pigment be deposited in the atrophied fat-cells, the tissue becomes yellow or yellowish-brown (**pigmentary atrophy**). See Flemming, "Archiv f. mikroskop. Anatomie," vii., and "Virch. Arch.," vol. lii.]

47. Atrophy may result from various causes. It has already been indicated (Art. 44) that the tissues may themselves possess inherent properties which determine their retrogression and decay. The efficient cause of this form of atrophy (described as **active atrophy**) is that the cells are no longer able to assimilate properly the nutriment brought to them. Atrophy like this, depending on internal conditions, seldom occurs as a pathological process. Only the so-called atrophy of inaction and trophoneurotic atrophy should perhaps be classed as pathological.

Atrophy of inaction occurs in organs that are subject to the direct influence of the nervous system, and perform their specific functions in obedience to nervous influence. Such are glands, nerves, and muscles. If a muscle or a gland be condemned to inaction for any length of time, it is apt to undergo atrophy. It is not unnatural to infer that the atrophy depends on the absence of functional activity in the cells, and to

frame the hypothesis that nutrition and functional activity go hand in hand and fall off together.

A typical instance of **trophoneurotic atrophy** is seen in the rapid disappearance of the muscles in cases where their proper nerves have been injured, or where there is disease of the anterior horns of gray matter in the cord. It appears that certain ganglion-cells in the anterior horns have a powerful influence on the nutrition of the muscles in connection with them. The disappearance of these cells, or the severance of their connection with the muscles, involves inevitably the atrophy of the latter.

Leaving these cases out of account, we may fairly refer all other forms of premature atrophy to defective nutrition. The process of the atrophy is the same whatever be the particular factor underlying the deficiency. This factor may be general anæmia, local change in the nutrient vessels, defective assimilation, or any other disorder of the kind; but it can at most determine the site and extent of the atrophy, not the process. Atrophy of this kind, occasioned by diminished nutrition, is distinguished as **passive atrophy**. Atrophy consequent on pressure is brought about, partly by mechanical hindrance of the cell-functions, partly by direct injury to the tissue, partly by interference with the circulation.

[Cohnheim ("Handbuch d. allgemeinen Pathologie") includes atrophy of inaction among the passive atrophies, and maintains that it depends on diminished blood-supply. It is not easy to believe that this explanation is in all cases adequate. Without undervaluing the importance of the blood-supply, there seems to be no objection to the theory that the assimilative power of an active working cell may be greater than that of one which is at rest.]

CHAPTER X.

CLOUDY SWELLING AND DROPSICAL DEGENERATION.

48. The term **cloudy swelling** or **parenchymatous degeneration** is due to Virchow ("Virch. Arch.," vols. iv., xiv.). He describes by it a certain swelling up of the elements of a tissue by imbibition or accretion; and defines it as a form of hypertrophy with a tendency to degen-

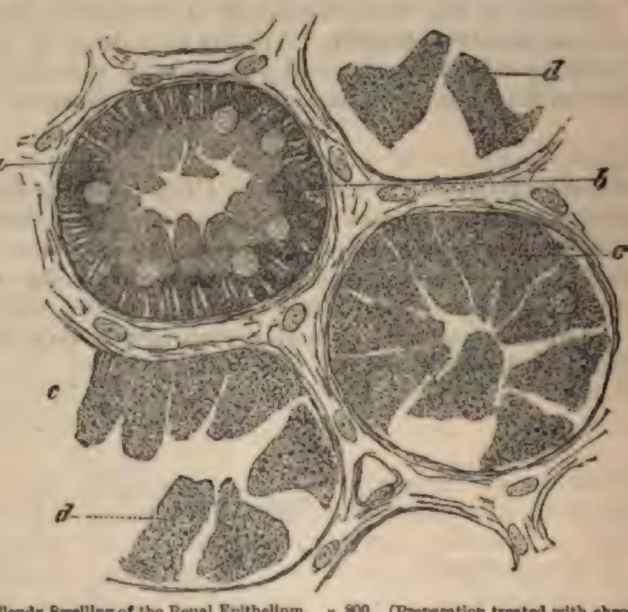

FIG. 6.—Cloudy Swelling of the Renal Epithelium. × 800. (Preparation treated with chromic acid and ammonia.) *a*, normal epithelium; *b*, cloudy swelling commencing; *c*, advanced degeneration: *d*, loose degenerate epithelium.

eration. The degenerative side of the process is the more important one. Histological investigation shows that the process consists in the formation of free granules in the substance of the affected cells, which may, for example, be those of the renal epithelium, of the liver, or of the heart-muscle. These free granules are to be regarded, from their microchemical reactions, as albuminoid bodies; they are soluble in acetic acid and insoluble in alkalies or ether. Their presence gives the cell a turbid

or cloudy appearance, and its normal form and structure quickly disappear. Thus in cloudy swelling of the renal epithelium (Fig. 6), the cells lose their longitudinal markings and the processes which normally project into the lumen of the tubule (*a*). The cell as it swells becomes rounder, and dark granules appear within it (*b*, *c*). The process depends on a degeneration of the cell-protoplasm. The cell becomes infiltrated with liquid, and a partial separation of its solid and liquid constituents takes place. The degenerative process often ceases when it has reached

Fig. 7.—Section through a "Mucous Patch" (*condyloma latum ani*). × 100. (Aniline-brown staining.) *a*, horny layer of the epidermis; *b*, rete Malpighii; *c*, corium; *d*, horny layer swollen up and infiltrated with leucocytes; *e*, swollen cells of the rete Malpighii; *f*, swollen epithelium infiltrated with cells; *g*, degenerate epithelial cells, into which leucocytes have made their way; *h*, granular coagula; *i*, swollen papilla, infiltrated with cells; *k*, corium infiltrated with cells and fibrin; *l*, lymphatic vessel; *m*, sweat gland.

a certain stage, and the cell returns to its former normal condition. In other cases, the cell-substance perishes and breaks up into granular detritus. Frequently the process is associated with fatty degeneration (Art. 50).

Cloudy or granular degeneration is of very common occurrence. It is found in the parenchymatous organs, such as the liver, kidneys, and heart, in most cases of infectious disease; but chiefly in scarlet fever, typhoid fever, small-pox, erysipelas, diphtheria, septicæmia, etc. The affected organs have a cloudy, dull, often grayish look; in the severer cases they look as if they had been boiled. They contain an abnormally small quantity of blood, and are doughy in consistence. The minuter structure of the organ is blurred or altogether destroyed.

There is a certain morbid change in connective-tissue cells which may be classed under this head. It is frequently observed in œdematous or inflamed connective tissue. The affected cells swell up, and dark spherules form in the nucleus as well as in the cell-protoplasm. These spherules, with which the cells are often tightly crammed, are distinguished by their power of taking up an intense color when stained, especially with aniline dyes ; in this they behave like micrococci. Their significance is not understood, though their formation may probably be regarded as evidence of a retrogressive change.

49. The term **dropsical degeneration** fairly describes a morbid change observed chiefly in epithelial cells. They imbibe liquid and become sodden and swollen. The process is near akin to cloudy swelling and degeneration, though the changes in the dropsical cells are of a somewhat peculiar nature. The imbibed liquid causes the cell to appear translucent (Fig 7, *e*). The granules of the protoplasm are pushed asunder, and often crowded toward the periphery ; so that the cell comes to resemble somewhat a vegetable cell (*f* and *g*). It becomes at the same time vacuolated, the spherical vacuoles containing clear liquid. The nucleus also swells up, and at length appears as a distended vesicle with clear contents. Changes of this kind may be seen in the cells of dropsical tissues and in inflammation. In inflammation it is chiefly the epithelial cells that exhibit marked changes (Fig. 7, *d*, *e*, *f*, *g*). In stained preparations the dropsical cells remain brighter than the healthy ones.

CHAPTER XI.

FATTY DEGENERATION.

50. If parenchymatous degeneration (Art. 48) go beyond a certain point, it often passes into **fatty degeneration**, that is to say, fat-globules form in the disintegrating cells. This variety of fatty degeneration is, however, of limited occurrence, compared with the other varieties to which the organism is liable.

Fat, as we know, occurs in the body in considerable amount even under normal conditions. Certain regions, and especially certain tissues of the fibrous type, like the subcutaneous and subserous structures, the marrow, etc., are always rich in fat. The fat is, as it were, stored up in these special regions, being either derived from without, or formed on the spot in the cells of the tissue itself. Increase of the quantity in store, whether due to increased supply or diminished expenditure, does not rightly come under the title of fatty degeneration. We distinguish it as **lipomatosis** (obesity, adiposity). Within limits it must be deemed physiological; when excessive it may pass into the domain of pathology. In such extreme cases, fat is found in cells which normally contain none. The fatty deposit takes the form of oily drops, which soon coalesce into larger spherules; until at length a single large fat-globule occupies the entire cell. Fatty infiltration of this kind affects chiefly the cells of the connective tissue in particular regions, and the liver-cells.

True fatty degeneration must of course be distinguished from lipomatosis or fatty infiltration. The fat which occurs in the former is not fat in store, so to speak; it is fat resulting from the disintegration of albumen in the affected cells. Inasmuch as fat is normally formed from the albumen of the cells, and is consumed as it is formed, we are driven to suppose that in fatty degeneration either the disintegration of albumen is increased, or the consumption of the fat produced is impeded. Both these things may occur, but it is specially to be noticed that in fatty degeneration the lost albumen is not replaced, so that the production of fat is associated with atrophy.

FIG. 8. — Fatty Degeneration of the Muscles of the Heart. + 350.

51. A cell undergoing fatty degeneration always shows larger or smaller oil-drops in its interior. These are colorless, bright, dark contoured, insoluble in acetic acid, soluble in alcohol and in ether.

In perosmic acid they stain black. The number and size of the oil-drops in the interior of a cell vary greatly; the size even of the largest is not usually great. Thus, for example, in fatty degeneration of the muscle of the heart, we find more or fewer according to the degree of the degeneration (Fig. 8). But they are all small and seldom coalesce into larger drops; they never form very large ones. In fatty degeneration of the kidney (Fig. 9) the appearances are similar; but the size of the oil-globules is not so regular (*c*, *e*).

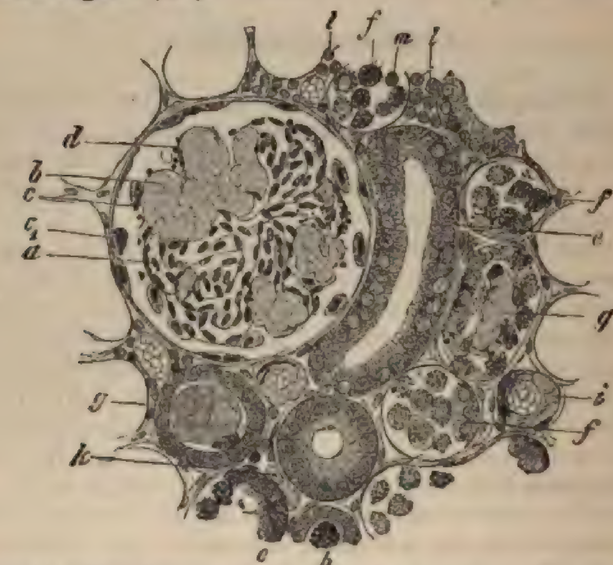

FIG. 9.—Amyloid and Fatty Degeneration of the Kidney. + 300. (Preparation treated with Müller's fluid and perosmic acid.) *a*, normal capillary loop; *b*, amyloid capillary loop (Art. 57); *c*, fatty epithelium of the glomerulus; c_1, fatty epithelium of the capsule; *d*, oil drops on the capillary walls; *e*, fatty epithelial cells *in situ*; *f*, loosened fatty epithelial cells; *g*, hyaline coagula (forming "casts"); *h*, fatty cast in section; *i*, amyloid artery; *k*, amyloid capillary; *l*, infiltration of connective tissue with leucocytes; *m*, round-cells (leucocytes) inside a uriniferous tubule.

When the degeneration becomes more advanced, the fatty epithelial cells are shed and become disintegrated (*f*). The oil-globules they contain are thus set free and accumulate in the tubules (*h*).

Fatty degeneration may occur in connective-tissue cells as well as in epithelial cells. If it affect entire cell-groups or systems, it may be recognized even by the unaided eye; and the more readily as the degeneration is more advanced, the proper color of the tissue less marked, and the amount of blood present less considerable. Colorless transparent structures, like the intima of the heart (endocardium) and great vessels, take on an opaque white appearance; the cortical tissue of the kidney becomes grayish white or, when the fatty change is greater, opaque yellowish white; the heart-muscle becomes yellowish; and voluntary muscle pale yellowish brown.

If complete disintegration of the tissue follow upon fatty degeneration, and if the mass of detritus lose water and become condensed, the

fatty change passes into caseation (Art. 39) ; and the tissue assumes a dull white cheesy appearance.

Like the cells of solid organs, the cells of organic liquids such as pus, and those of coagulated exudations, very often undergo true fatty degeneration ending in their complete destruction as cells.

[In tissues undergoing fatty degeneration, as also in liquids whose cells are degenerating, there are very frequently found cells crammed full of fat-granules. They are referred to as "fat-granule cells." Their origin is only in part traceable to fatty degeneration of the cells themselves. They are rather to be looked upon as migratory corpuscles which have taken up the fatty products of disintegration, and so have become transformed into granule-carriers (Art. 114). See Reinhardt, "Virch. Arch.," vol. i.]

52. The **cause** of fatty degeneration is to be sought in an alteration in the constitution of the blood, *i.e.*, of the nutriment supplied to the cells. Deficient supply of oxygen plays a chief part in it. To this must be ascribed, on the one hand, the disintegration of albumen and the formation of fat ; on the other hand, the fact that the fat produced is not straightway consumed.

If to the lack of oxygen there is added a deficiency of proper nutriment, so that the albumen which is used up by transformation into fat is not replaced, the amount of albumen in the affected part must of course diminish.

Corresponding to the case just indicated, we find fatty degeneration taking place in conditions which are associated with general or local anæmia. For example, if the blood becomes diseased in such a way (anæmia, leukæmia) that its power of taking up oxygen is diminished, and its nutritive value lowered, fatty degeneration is found to occur in the most widely different organs. The same thing comes to pass in particular organs which happen to receive too little blood, either in consequence of disease in the afferent vessels, or because the outflow of blood from them is checked and its renewal hindered. Lastly, organs like the muscles which for any reason are left unexercised, and so fail to undergo an adequate amount of tissue-change, are very apt to become fatty.

Various poisons, such as phosphorus, arsenic, and the ferments which produce fevers, may, like imperfect oxygenation, lead to disintegration of the albumen of the tissues and so to fatty degeneration.

[We still seem far distant from an exact understanding of the origin and the ultimate fate of the fat which is formed in the body in physiological and pathological conditions. Hoppe-Seyler ("Physiolog. Chemie") inclines to think that fat cannot be formed directly from albumen. He regards it as not unlikely that glycogen is first formed, and from the glycogen fat. Voit ("Zeitschr. f. Biol.," v., and "Neues Rep. f. Pharmacie," xx.), on the other hand, thinks it quite certain that fat may be formed at once from albumen ; compare Quain, "Medico-Chir. Trans.,"

vol. xxxiii. According to Hermann, it is probable that certain products derived from the disintegration of albumen are normally utilized in regenerative processes. If the oxygen needed for regeneration is wanting, these products cannot be utilized and disintegrate still further ; the expenditure of fresh material is thus increased. Binz and Schulz ("Arch. f. exper. Path.," vol. xiv.) hold that the cells, in their avidity for oxygen, take it up from the blood so long as the blood continues to part with it ; when it ceases to do so the cells attack each other, and act as mutual reducing agents. The lateral "chain" of the albumen-molecule (the chain which includes the nitrogen, on the theory of these chemists) is thus broken ; the consequence is increased production of urea and of fat. They explain in this way the fatty changes observed in carbonic oxide poisoning. Bence Jones ("Lectures on Pathology, etc.") accounts for the proneness of the liver to become fatty in a somewhat similar way. See also Ranvier ("Société anat.," 1868).

On the effect of phosphorus in inducing fatty change, see Voit and Bauer ("Zeitschr. f. Biol.," vii.), Lewin ("Virch. Arch.," vol. xxi.), Ranvier ("Soc. de Biologie," 1866).]

53. It is generally, though not always, easy to decide whether the fat present in the cells of an organ is a product of degeneration, or simply a deposit by way of storage. It is commonly stated that the fat of degenerative atrophy appears in the form of minute non-coalescent drops ; while deposited fat occurs in large drops which readily run together. This is true of most tissues, but not of all. It is true, for example, of striated muscle, heart-muscle, non-striated muscle, neuroglia, etc. But when the renal epithelium becomes fatty, fat-globules of very considerable size are sometimes formed. In the liver again, the fat of degeneration may form either small or large drops (the latter in phosphorus-poisoning).

On the other hand, what we may call storage-fat is, in the first instance, deposited in very minute globules ; while the great globules of fatty deposits, when about to undergo reabsorption, break up again into minuter globules.

But if the distinction is not always clear from the histological appearances, we may get more certain information by considering the site in which the fat is found. The appearance of fat-globules in tissue-cells normally free from fat, in circumstances which preclude the idea of a determination of fat to the tissue, is evidence that fat has been formed *in loco* from the cell-albumen, and therefore that the cells have so far become disintegrated. Difficulty can thus arise only in the case of organs, such as the liver, which may normally be the seat of fatty deposit, and on the other hand are prone to fatty degeneration. In such organs it is often hard to say how much of the fat they contain has been produced *in loco*, how much has been brought to them from without. There is a further complication, for the fat of degeneration is sometimes carried

away from its original seat, and deposited in other spots in the form of a fatty infiltration, or of storage-fat.

54. When fat is present in considerable quantity it happens not infrequently that crystalline products separate out from it. The so-called "fat-crystals" appear as feathery needles, grouped together in tufted bunches (Fig. 10, *b*). They are often described as needles of **margaric acid**. Whether they really contain margaric acid is doubtful. It is known that equal parts of palmitic and stearic acid would give a mixture having the same composition as is ascribed to margaric acid; and further that palmitic, stearic, and oleic acids in combination with glycerin (as tripalmitin, tristearin, and triolein) form the chief components of ordinary animal fat. It is therefore doubtful whether margaric acid or trimargarin really exists as a distinct component of animal fat at all. These fat-crystals may form in fatty products of disintegration as well as in normal fat-cells. In the latter case they are only produced *post-mortem*.

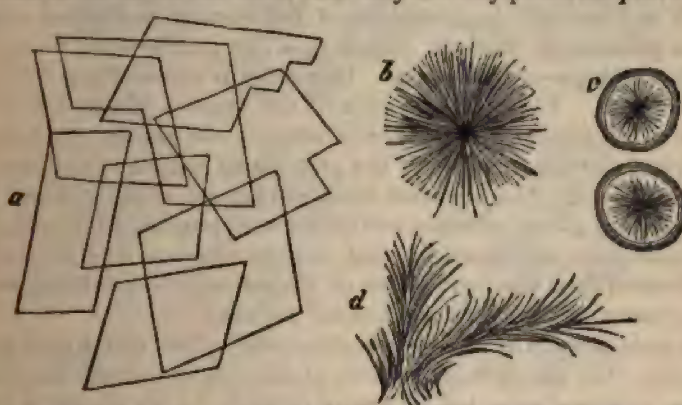

FIG. 10.—Fat Crystals. × 200. *a*, cholesterin-tablets; *b*, free tuft of margarin-needles; *c*, tuft inclosed in fat-cells; *d*, feathery needles of "margaric acid" or margarin.

In masses of fatty detritus it is very common to find what is called **cholesterin** (properly cholestearin). This forms thin transparent rhombic tablets (Fig. 10, *a*), often notched at the angles. If these tablets are present in quantity, they may often be recognized by their lustre with the naked eye alone. They are soluble in hot alcohol, ether, and chloroform, in oils, and in the sodium compounds of the two bile-acids (glycocholic and taurocholic). Treated with sulphuric acid the crystals become purplish red, rusty, or violet at their edges. The same coloration appears still better on treatment with iodine. Nothing is known of the mode in which cholesterin is formed. It is said to exist as a normal constituent in the brain (Gamgee).

[Schulze and Barbieri ("Journ. f. prakt. Chem.," 25, 1882) regard cholesterin as an intermediate product of vegetable metabolism and a constant component of vegetable cells. Cholesterins of various composition are known, so that the term seems to indicate rather a chemical *genus* than a definite substance.]

CHAPTER XII.

MUCOID AND COLLOID DEGENERATION.

55. The **mucoid degeneration** of the tissues has its physiological type in the mucus-secretion of the mucous membranes and mucous glands.

As is well known, the epithelium of the mucous membranes contains so-called goblet-cells (Eimer). These look like goblets filled to overflowing with a transparent substance. This latter is mucus formed from the cell-protoplasm. The epithelial cells of the mucous glands are similar. They swell up when about to secrete mucus; the central parts become transparent, and the granules of the protoplasm become aggregated into groups or strings. The so-called mucus-corpuscles in the salivary secretion, with their glassy contents and tremulous granules, are merely leucocytes which have undergone mucoid metamorphosis. The mucous substance formed from the protoplasm of the cell may be extruded, and the cell may recover; in other cases the cell perishes.

The same process of mucus-formation takes place under pathological conditions. For example, in catarrh of the mucous membrane we find that the increased secretion of mucus depends on an increased mucus-forming power in the lining epithelial cells, as well as in the cells of the mucous glands. Investigation shows that in cylindrical epithelium the goblet-cells (Fig. 11, 6) are increased in number. In the secretion also we may find cells in a state of complete mucoid degeneration; they are transformed into glassy masses containing a few scattered granules (3 and 5). In other cells (7) the mucus may take the form of lumps of various sizes, enclosed within the unchanged cell-protoplasm.

The epithelia of pathological tissues may, like the normal ones, undergo mucoid change. Typical goblet-cells are occasionally found in the epithelial lining of ovarian and intestinal cysts. In certain forms of cancer, the majority of the epithelial cells undergo mucoid degeneration.

The fibrous tissues, like the epithelia, are also liable to undergo mucoid degeneration. Thus connective tissue, cartilage, bone, adipose tissue, marrow, sarcomatous tissue, may all become mucoid, and so assume a jelly-like translucent appearance. In these tissues it is usually the ground-substance which is transformed. The fibrous constituents lose their structure and become homogeneous. The tissue-cells may persist,

or become fatty, or they may take part in the mucoid change. The final product is a hyaline mass recalling the original tissue only by virtue of a few stray fibrous shreds, or single cells, or groups of cells, scattered through it.

Mucus swells up readily in water; acetic acid makes it coagulate; alcohol makes it turbid, white and opaque.

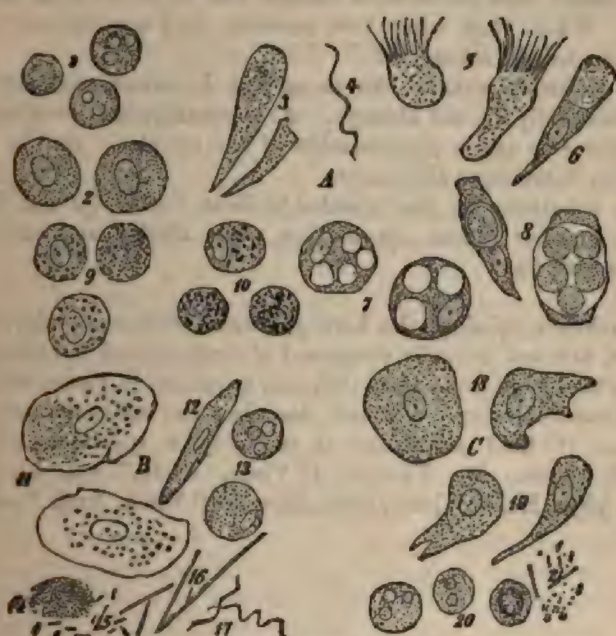

FIG. 11.—Catarrhal Secretions from various Mucous Membranes. + 400. *A*, from cylindrical epithelium; *B*, from the mouth; *C*, from the bladder. 1, round-cells (pus corpuscles); 2, large round-cells with clear nuclei from the nose; 3, mucoid cylindrical cells from the nose; 4, *Spirillum* from the nose; 5, mucoid ciliated cells from the nose; 6, goblet-cell from the trachea; 7, round-cells with mucus-masses from the nose; 8, epithelial cells containing pus corpuscles from the nose; 9, fatty cells in chronic laryngeal and pharyngeal catarrh; 10, cells from sputum containing soot-pigment; 11 and 12, squamous epithelium from the mouth; 13, mucus-corpuscles; 14, micrococci; 15, *Bacterium termo*; 16, *Leptothrix buccalis*; 17, *Spirochæta denticola*; 18, superficial cells from the bladder; 19, deeper layer; 20, pus corpuscles; 21, *Schizomycetes* or bacteria.

56. **Colloid degeneration** is closely akin to mucoid degeneration; for here too the essence of the process is the metamorphosis of an albuminoid substance. The details of the chemical changes which occur are not known. The material which constitutes the colloid substance is derived from the epithelial cells. In aged persons, a certain amount of colloid change in the thyroid gland may be regarded as physiological. The parenchyma of the gland is full of large and small spherules, which on section have a translucent sago-like appearance. They are generally yellowish or brownish in color, and of the consistence of firm jelly. If the colloid change has gone on to a pathological extent, this translucent substance may form the greater part of the mass of the gland. It may even lead to a marked increase in its size, forming a colloidal goître. Microscopic

examination shows that the colloid mass is homogeneous. It encloses but few cellular elements, and these for the most part at the periphery, where the colloid change is in progress. Sometimes a large continuous patch of degenerate tissue may be produced by the coalescence of smaller ones. The formation of the colloid substance is indicated by the appearance of minute homogeneous spherules in the cells of the acini. These spherules escape from the cells, or become free when the cells themselves break up. When they come into contact, they coalesce to form the homogeneous colloid substance.

Colloid spherules, exactly like those just described, are found in the tubules of morbidly altered kidneys. At times large masses of coalescent spherules occur in cystic degeneration of the tubules. In the prostate gland similar formations also occur.

Colloid substance is distinguishable from mucus by the fact that acetic acid does not induce coagulation, while alcohol and chromic acid produce no turbidity.

[In Virchow's opinion, the homogeneous spherules, while contained in the cells, are not actually composed of true colloid substance. The latter is formed from them after they run together, in virtue of a special chemical transformation. Virchow describes the spherules as modified protoplasm. Colloid substance is probably a resultant of several albuminoid bodies. See Virchow ("Virch. Arch.," vol. i.), Wagner ("Arch. f. phys. Heilk.," 1856, 1866), Eberth ("Virch. Arch.," vol. xxi.).]

CHAPTER XIII.

AMYLOID DEGENERATION AND AMYLOID CONCRETIONS.

57. **Amyloid degeneration** is a peculiar degenerative process, which is apt to affect the connective tissues, and is progressive in character. It leads to the deposit of a special albuminoid body (the amyloid substance) in the affected tissues; these therefore increase in bulk and assume under the microscope a peculiar uniform semi-translucent appearance. The affection may occur in any of the organs, but it is specially common in the spleen, liver, kidneys, intestines, and lymphatic glands.

When sufficiently intense the morbid change is recognizable with the naked eye; the part looks semi-translucent, so that it is described as "waxy" or "lardaceous," *i.e.*, like the fat of fried bacon. If the change is confined to scattered patches, as it often is in the spleen, these look like grains of boiled sago or tapioca; hence the name "sago-spleen." In other cases, the process affects the spleen-tissue uniformly. The whole organ grows large and firm to the touch, while the section presents the peculiar translucent lardaceous appearance. Like appearances are found in the liver. The kidneys, too, may undergo considerable increase in size, and present in patches or throughout the lardaceous character, becoming at the same time firmer in consistence. In other cases the translucent patches are so small as not to be readily noticed; the possible presence of amyloid substance is, however, often indicated by changes of another kind, such as fatty degeneration. In the intestine the degeneration is seldom recognizable without optical or chemical examination. The same is true of the organs that are less liable to the change, such as the heart, the great vessels, the thyroid gland, etc.

58. The amyloid substance so deposited in the tissues in uniform shiny patches exhibits a peculiar reaction with iodine, and with some of the aniline colors. A solution of iodine in water, or better in potassium iodide and water, when poured on the tissue to be tested, stains the amyloid substance a dark brownish red or mahogany color. If added to a section under the microscope the staining is a bright brownish red, while the unaffected tissue remains pale yellow. Where the degeneration is extreme, the tissue may become almost woody in consistence, and then the staining may be violet or blue or greenish. If the ordinary iodine-stained tissue be treated with very dilute sulphuric acid, the amyloid

patches take on a darker brown, or become violet, blue, or greenish; but the reaction is generally imperfect. Methyl-aniline or aniline-violet stain the amyloid substance bright ruby-red, and the healthy tissue blue or dark indigo.

The peculiar iodine-reaction was first observed by Virchow, the discoverer of the amyloid substance. This reaction led him to consider the amyloid substance as a non-nitrogenous body allied to cellulose and starch. Cellulose, when treated with iodine and strong sulphuric acid, is stained bright blue. Starch with iodine alone gives an ultramarine tint. For this reason Virchow called the new body "amyloid." It was not until some years later that Friedreich and Kekulé proved the amyloid substance to be nitrogenous, to be, in fact, an albuminoid body. The special reaction of the amyloid substance enables us to detect its presence in the tissues, even when to the eye it is not differentiated from them. In examining fresh specimens in a cursory way, the only precaution necessary is to see that the surface is washed free from blood; the red color of the blood blended with the yellow of the iodine may simulate the characteristic brownish-red staining.

The amyloid substance is very slightly acted on by acids or alkalies. Alcohol and chromic acid do not alter it at all; and it has the power of withstanding putrid decomposition for a long time. It is not dissolved by gastric juice at the temperature of the body.

[Amyloid degeneration was not altogether unknown before Virchow's researches. Rokitansky had previously introduced the names bacon-liver or lardaceous liver, waxy liver, bacon-spleen, sago-spleen. But it was Virchow who first investigated the nature of the amyloid substance, first of all in amyloid concretions (Art. 61), afterward in degenerated tissues; and he discovered the iodine reaction ("Virch. Arch.," vols. vi., viii.). Friedreich and Kekulé first showed that the substance was nitrogenous ("Virch. Arch.," vol. xvi.), which was confirmed by Rudneff and Kuehne ("Virch. Arch.," vol. xxxiii.). The literature of the subject is fully given by Kyber, who has also made numerous additions to our knowledge regarding its occurrence ("Die amyloide Degeneration," Dorpat, 1871, and "Virch. Arch.," vol. lxxxi.). Jürgens first described the color-reaction with iodized methyl-aniline ("Virch. Arch.," vol. lxv.); Cornil studied the reactions with other aniline colors ("Arch. de physiol.," 1874). Dickinson showed that a characteristic blue color is imparted to the amyloid substance by sulphate of indigo.]

59. The amyloid substance is either formed or deposited in the fibrous textures of the blood-vessels, and in the walls of the smaller vessels especially.

If a microscopic section of an amyloid liver be so treated as to bring out the minuter changes in its structure, it is not hard to show that the seat of the affection is in the capillary walls, that is, in the peri-endothe-

lial fibrous tissue. The endothelium is thickly coated on its outer aspect with a uniform glassy layer, here and there broken up into lumps (Fig. 12); this is the amyloid deposit. The liver-cells may remain unchanged between the amyloid masses, or they may be misshapen and partly atrophied. They very often contain fat. If the afferent vessels be examined, it will be found that they too exhibit amyloid patches, especially in their middle coat.

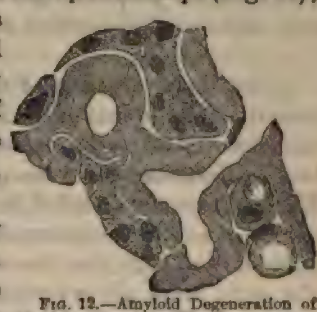

FIG. 12.—Amyloid Degeneration of Liver Capillaries. × 300. (Section treated with perosmic acid.)

The appearances in an amyloid kidney are exactly similar (Fig. 13). A good section shows as before that the formation of the homogeneous deposit occurs mainly in the vessel-walls. The walls of the vascular loops in the glomeruli (*b*), are greatly swollen and homogeneous in structure, and the arteries (*i*), veins, and capillaries (*k*) of the parenchyma show traces of amyloid deposit.

In other parts, such as the intestinal mucous membrane, the appearances are of the same kind. The vascular system, however, is not invariably the chief seat of deposit; the connective tissue is often chiefly and

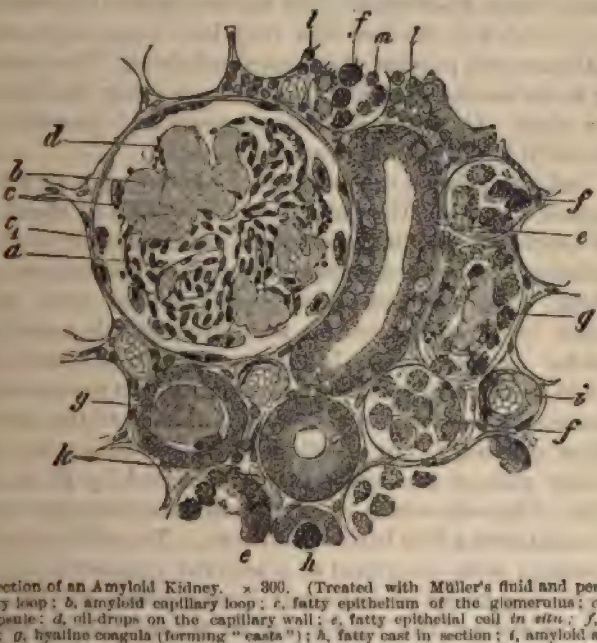

FIG. 13.—Section of an Amyloid Kidney. × 300. (Treated with Müller's fluid and perosmic acid.) *a*, normal capillary loop; *b*, amyloid capillary loop; *c*, fatty epithelium of the glomerulus; c_1, fatty epithelium of the capsule; *d*, oil-drops on the capillary wall; *e*, fatty epithelial cell *in situ*; *f*, loosened fatty epithelial cells; *g*, hyaline coagula (forming "casts"); *h*, fatty cast in section; *i*, amyloid artery; *k*, amyloid capillary; *l*, infiltration of connective tissue with leucocytes; *m*, round-cells (leucocytes) inside a uriniferous tubule.

directly affected. In the lymphatic glands and the spleen (Eberth), it is the fibrous trabecular network which suffers most; in striated muscles the

perimysium internum and the sarcolemma (Ziegler). In glandular organs with a *tunica propria* (*e.g.*, the mucous glands and kidneys), this latter may undergo degeneration and become greatly thickened.

[The above account of the common seat of amyloid deposit differs essentially from that given in various text-books (*e.g.*, Rindfleisch's) and memoirs. Most authors assert that in glandular organs the chief seat of amyloid formation is in the gland-cells, that is, in the epithelial elements. Ziegler has not succeeded in convincing himself that this is the case. In no one of seven specimens of amyloid liver could he find, on the carefullest examination, that the liver-cells had undergone amyloid degeneration. The cells were always recognizable, though at times greatly atrophied and compressed by the interposed deposits. The examination of mucous glands and kidneys yielded like results. He is therefore constrained to agree with Wagner ("Arch. d. Heilkunde," ii., 1861), Eberth ("Virch. Arch.," vol. lxxx.), Heschl ("Wiener Sitzungsberichte," vol. lxxiv.), and others—who regard the connective tissue as the primary seat of amyloid formation, and deny that the epithelium is commonly concerned in it. Ziegler does not go so far as to say that epithelial cells are incapable of amyloid change; but he is sure that even in extreme cases of amyloid disease they may remain unaffected. The notion that the liver-cells are commonly affected is due to the fact that they have been overlooked among the amyloid flakes and patches which surround them. The iodine method is probably to be blamed for this, for it fails to bring the liver-cells distinctly into view. Ordinary staining-reagents and perosmic acid are much more useful in this respect than iodine.

Ziegler had recently an opportunity of examining a very interesting case of amyloid disease. The patient was a woman of about fifty, who had died of heart-failure. On post-mortem examination it was found that the heart, all the mucous membranes, the peritoneum, tongue, and lungs were amyloid. The pericardium and endocardium were everywhere thickened and beset with numerous translucent gristly nodules as large as millet-seeds. Similar nodules in vast numbers were found in the peritoneum, and in lesser number in the heart-muscle, the *muscularis mucosæ* of the intestine, the *mucosa* and *submucosa* of many of the mucous membranes, and in the lungs. In addition to these nodules the heart-wall (and especially that of the auricles) was traversed by thick seemingly fibrous bands. The *submucosa* of the small intestine was for the most part transformed into a firm bacon-like tissue. The nodules and also the dense thickenings were composed of a uniform substance, either structureless or showing traces of coalescent homogeneous blocks. This was deposited in the walls of the vessels, and in the connective tissue. The vessel-walls were in some places thickened ten- to twenty-fold. When the margins of the affected patches were examined microscopically, it seemed as if the homogeneous substance had been directly produced from the ground-substance of the connective tissue, by a process of swelling

other the epithelial elements of the organ become secondarily dis-

Amyloid change is essentially a degeneration. The connective are permanently altered, for the amyloid substance being but ly soluble does not disappear again when once deposited. It is ob- that a foreign element of this kind must seriously interfere with the ons of the affected organs, such as the kidney, or intestine.

e morbid change in the vessel-wall often leads to narrowing and e of the vessel, and so to permanent disturbance of the circulation. are not without effect on the epithelial elements; they speedily e fatty. And inasmuch as the fibrous framework of the organ is at ame time increasing in size and volume, the gland-cells are com- d and so tend to disappear altogether. In the liver such misshapen trophied cells, as well as others in a state of fatty degeneration, are often met with. In the kidney the fatty changes in the epithelium 13, *e*, *f*) form a striking and characteristic accompaniment of amy- egeneration.

the spleen and lymphatic glands the lymphoid cells are likewise apt ish, atrophied and fatty, under the pressure of the swollen and al- trabecular network. In muscle the contractile substance vanishes, amyloid masses in the connective tissue increase and multiply.

. Amyloid degeneration, as above described, is generally a process ing several organs at the same time; or when it happens to affect one, it takes the form of a change extending throughout the entire . But in addition to this diffused form we find a more local one, nting the appearance either of circumscribed foci of degeneration, **amyloid concretions.**

ese localized amyloid formations occur, so far as we know, only in s which have already undergone morbid change. They are espe- apt to follow in the wake of inflammations, either early in the s of granulation, or later when cicatricial tissue has been formed. are also found in tumors which are undergoing retrogressive e. Small single foci may be formed in the affected tissue, or they

In many cases homogeneous bodies exhibiting the amyloid reaction are obviously formed in the exudation-products of inflammation or hemorrhage. For example, the so-called tube-casts of the kidney, formed in the tubules by a singular transformation of transuded liquid and shed epithelium, show not infrequently the amyloid reaction if they have lain long *in situ*. In the remains of old hemorrhages amyloid bodies have often been found (Fig. 14, *b*). They often enclose a foreign substance, such as a crystal of hæmatoidin. These bodies are called amyloid concretions or *corpora amylacea*. They are found under normal conditions in the central nervous system, especially in the ependyma of the ventri-

FIG. 14.—Corpora Amylacea. + 400. *a*, stratified concretion from the prostate; *b*, *corpus amylaceum* from an old hemorrhagic infarct of the lung; *c*, *corpora amylacea* from the spinal cord.

cles. It was here that Virchow first discovered them. They take the form of small more or less clearly stratified spherules (Fig. 14, *c*). At times they may be found abundantly in morbidly altered brain-substance, and in cerebral tumors. Corpora amylacea are also very common in the prostate gland. They lie in the lumen of the acini and are of considerable size; often indeed they may be recognized by the naked eye as brown grains upon the surface of a section. They are distinctly stratified (Fig. 14, *a*), except toward the centre.

These localized amyloid formations, and especially those originating in tube-casts and old extravasations of blood (Fig. 14, *b*), serve to prove that amyloid substance may arise from a direct metamorphosis of the albumen of blood and of epithelium. The prostatic concretions, when they really are amyloid (and this is not always the case), are probably to be regarded as modified cell-products.

[A large number of memoirs have dealt with the question of localized amyloid change. Kyber (*loc. cit.*), Leber ("Arch. für Ophthalm.," xix., xxv.), Hippel (*ibid.*, xxv.), von Becker ("Amyl. degen. tarsi," Helsingfors, 1876) refer to amyloid formations in the eyelid. Friedreich ("Virch.

Arch.," vols. ix.,) x. and Zahn (*ibid.*, vol. lxxii.) found amyloid bodies in the lung; Langhans in cancer-nodules (*ibid.*, vol. xxxviii.); Burow (" Langenbeck's Arch.," xviii.) in tumors of the larynx, etc. On prostatic concretions see Paulizky ("Virch. Arch.," vol.xvi.). Ziegler discovered amyloid bodies in syphilitic scars (" Virch. Arch.," vol. lxv.), in a hemorrhagic infarct of the lung which had healed, and in a cancer of the stomach.

62. As to the **causes** and the nature of **amyloid degeneration,** there is little to say that is quite definite or quite certain. We know, of course, in what circumstances it is apt to occur, namely in cachectic conditions of the system. On the other hand, we do not know to what alterations in normal metabolism the morbid process owes its special character. The forms of cachexia which lead to extensive amyloid change are in particular tuberculosis, syphilis, chronic destructive ostitis or periostitis, chronic dysentery (cœliac flux), and leukæmia; while the cancerous cachexia seldom tends to favor it. Amyloid degeneration may, however, occur without previous disease. Some of Cohnheim's researches show (" Virch. Arch.," vol. liv.) that the degeneration may become developed in two to three months.

Amyloid change extending to several organs is a local disorder conditioned by general causes. The amyloid substance does not exist in the blood, yet the material out of which it is developed is derived from the blood. It would appear that reduced vital activity of the tissues dependent on general cachexia favors the formation of the substance. We may, perhaps, provisionally picture to ourselves the formation of this peculiar substance, as due to a combination of an albuminoid body from the blood with certain components of the tissues; or we may regard it as a modification of the albumen of the blood, separating out from the latter in consequence of some abnormal metabolism in the cachectic patient.

In local amyloid formations, the substances metamorphosed are partly albumen from the blood (concretions formed in extravasations), partly albumen derived from epithelial cells (tube-casts and prostatic concretions). In the latter case the special metamorphosis is effected, without the co-operation of living tissue, in albumen which has lain for a time in the tissues without being of them. Here the conditions must be of a purely local nature.

[Virchow (" Cellular Pathology") and Kyber (" Virch. Arch.," vol. lxxxi.) have compared the amyloid degeneration of tissues to the process of chalky deposit, and the comparison seems a good one. In both cases we probably have a tissue whose nutrition is somehow lowered; a substance brought to the tissue by the blood; and an intimate combination between this substance and a substance pre-existing *in loco.* Wagner (" Handbuch d. allgem. Pathologie," 1874, p. 417) considers the lardaceous material we have described to be due to a retrogressive metamorphosis of albuminoids, forming in fact an intermediate stage between these bodies and fat. Dickinson argues that it is of the nature of fibrin (blood-

albumen) "modified by loss of alkali or gain of acid" ("Trans. Path. Soc.," 1879).

A statistical analysis of the causes of amyloid degeneration is given by Hennings ("Inaug. Diss., Kiel," 1880). He makes out that phthisis and suppuration of bone hold the first rank among the etiological conditions. The spleen is oftenest diseased; after that follow in order the kidneys, liver, intestine, stomach, suprarenal capsules, pancreas, lymphatic glands, thyroid gland, aorta, lungs, ovaries, uterus. Somewhat similar analyses are given by Fagge ("Trans. Path. Soc.," 1876) and Turner (*ibid.*, 1879).]

CHAPTER XIV.

HYALINE DEGENERATION OF THE FIBROUS TISSUES.

63. **Hyaline** (or vitreous) **degeneration** of the fibrous tissues resembles amyloid degeneration in its superficial appearance as well as in its seat; but it does not give the special and peculiar reactions of the amyloid substance. It occurs chiefly in the adventitious tissue of the arteries. The adventitia becomes transformed into a shining, translucent, strongly refracting substance, increasing at the same time in thickness. Water has no effect on this substance; iodine stains it pale yellow; ether and chloroform give no reaction. It thus resembles in many respects the colloid substance. It is specially common in the vessels of the brain and of the lymphatic glands (Wieger). Apart from the blood-vessels a hyaline thickening is also observed in the stroma of tumors, in inflammatory hyperplasias, especially in those of hereditary syphilis (such as occur in the liver, for example), and in structureless membranes like the hyaloid membrane of the eye. As to the nature of the change nothing is known. Disturbances of the circulation (Wieger), and inflammations of the affected regions, have been mentioned as exciting causes.

[Wieger, under the guidance of von Recklinghausen, has lately examined and described the hyaline degeneration of the lymphatic glands ("Virch. Arch.," vol. lxxviii.). It seems to be very common in these organs. Memoirs on the hyaline degeneration of the cerebral vessels have been published by Arndt ("Virch. Arch.," vol. xli.), Neelsen ("Arch. d. Heilkunde," xvii.), Eppinger ("Vierteljahrsschrift f. pract. Heilk.," Prague, 1875), Lubimoff ("Arch. f. Psychiatrie," 1874), and others. The degeneration is found in the central nervous system in connection with various disorders.

Peters has quite recently ("Virch. Arch.," vol. lxxxvii.) made a series of researches in von Recklinghausen's laboratory on hyaline degeneration, and he manages to bring under this head all sorts of diverse changes and processes. Thus he includes under it inflammatory coagulations within and without the blood-vessels, coagulative necrosis of the epithelia in diphtheritic inflammation, homogeneous coagulation in exuded fluids, the formation of false membranes, the mucoid metamorphoses of the epithelial cells of mucous membrane, and thrombi in lymphatic vessels,

—in brief everything that has a hyaline look. This is a mere uncritical agglomeration of things that have nothing in common. We may perhaps be unable to distinguish with certainty the exact chemical and physical processes which lead to the formation of homogeneous masses in the various tissues and liquids ; but this does not justify us in affirming that no distinction is at all possible.

The case referred to in Art. 59 has great interest, as bearing on the discrimination of hyaline degeneration in fibrous tissues. It shows that hyaline change is near akin to amyloid change ; and that in the former as in the latter an albuminoid may be deposited in the tissues in the form of solid lustrous masses. Whether the hyaline degeneration of the vessel-walls, observed in various conditions, has always the same significance —is as yet an open question.

Gull and Sutton ("Medico-Chir. Trans.," 1872) have described a "hyalin-fibrous" degeneration of the blood-vessels in connection with chronic renal disease. Klein ("Trans. Path. Soc.," 1877) has described and figured hyaline changes in the arterioles in typhoid fever and in scarlatina.]

CHAPTER XV.

INFILTRATION OF THE TISSUES WITH SALTS.

64. **Petrification** or **incrustation** is a process of transformation aracterized by the deposit in a tissue of various salts derived ultimately om the blood.

In by far the greater number of cases the deposit consists of carbon-es and phosphates of calcium, with a small quantity of the magnesium te ; it is in fact calcareous or chalky.

As we know, calcareous deposition takes place in special regions as a rmal physiological process. The formation of true bone is always pre-ded by the deposit of calcareous salts in the cartilaginous structures st laid down. This deposit takes the form of minute granules, which magnification look like grains of dust or irregular crumbs, and they e seen to lie chiefly in the matrix-substance and cell-capsules of the car-age. If the grains lie thick together, they give the part a whitish lor and a firm consistence.

In the same way as under normal conditions, but in the most various gions of the body, we may have a morbid deposition or precipitation of lcareous salts in the tissues. Experience shows that the tissues af-cted are either already necrosed, as in the case of caseous lymphatic lands, dead parasites, thrombi, and dead fœtuses (lithopædia),—or have een seriously stinted in their nutrition. This latter is the case in fatty degeneration of the tunica media of the arteries, or in fatty degenera-tion of tumors such as uterine fibroids. The cause of calcareous depos-ts is thus a local one. The calcium-salts dissolved in the blood are not simply precipitated and retained by the tissue, but they proceed to form solid compounds with the albuminoids.

Commencing calcification is not recognizable by the naked eye. When the deposit becomes more dense the tissue turns white. At the same time it often becomes extremely hard and cannot be cut with the knife. In other cases it becomes in color and consistence more like mortar.

[Litten affirms (" Der hæmorrhagische Infarct," 1879) that calcifica-tion depends on a necrotic modification of albumen, possessing a special chemical affinity for lime-salts. Kyber asserts (" Virchow's Archiv," vol. lxxxi.) that the lime-salts combine with the fatty acids, as well as with the albuminoids.]

65. Calcification invades the cells of a tissue as well as the ground-

substance. Thus ganglion-cells (Fig. 15) which have ceased to live in consequence of some brain-affection may become impregnated with lime-salts. Shining calcareous spherules are formed, which fill out the contour of the cell and its prolongations.

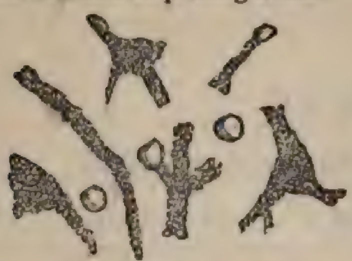

FIG. 15.

FIG. 16.

FIG. 15.—Calcified Ganglion Cells. (From the brain of a hemiplegic idiot with unilateral hydrocephalus.)
FIG. 16.—Calcification of the Tunica Media of the Aorta.

When an artery is affected, the cells as well as the ground-substance become calcified. Small shining granules are deposited in the latter, which at length thickly infiltrate the tissue (Fig. 16). Simple calcification does not produce any alteration in the apparent structure. The tissue is petrified as it stands, so to speak, without destruction or transformation of its form and texture. It is thus easy to distinguish histologically between calcification and ossification.

In tissues altered by inflammation, such as tuberculous lymphatic glands, fibrous false membranes or adhesions, as well as in certain tumors of the brain (psammomata), we find at times so-called **chalky concretions.** They are stratified bodies having an organic basis, in which lime-salts have been deposited. Fig. 17 represents some of these concretions: *a*, comes from an omentum thickened and deformed, and adherent, in consequence of chronic inflammation; *b*, from a tuberculous lymphatic gland. The several layers of the stratified concretion have a uniform shining appearance.

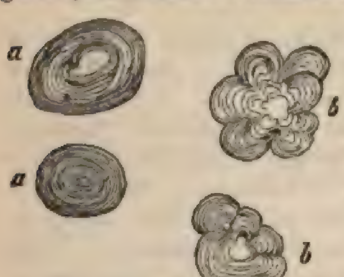

FIG. 17.—Chalky Concretions. *a*, concretions of an inflamed omentum; *b*, from a lymphatic gland altered by inflammation.

66. In **gout** we find deposits of urates, chiefly of urate of sodium, together with carbonates and phosphates. The deposition is apt to occur paroxysmally, especially in the metatarso-phalangeal joint of the great toe, but not infrequently in other joints also. Shining white masses (chalk-stones or tophi) are thus formed in the ligaments and cartilages of the joints, and even in the bones. These may also occur in the arteries, endocardium, skin, and kidneys. The deposit is usually in the form of needle-like crystals (Rindfleisch), or amorphous granules. It is said that the cells are the first to exhibit the deposit, the ground-substance being invaded secondarily (Cornil and Ranvier).

CHAPTER XVI.

FORMATION OF PIGMENT IN THE TISSUES.

67. The fibrous as well as the epithelial tissues, in certain regions, contain a **normal pigment.** It lies within the cells in the form of yellow, brownish, or black granules ; or the cells may seem more or less uniformly impregnated and stained. Of the pigmented epithelia the best examples are the deepest layer of the rete Malpighii, and the retinal epithelium. In the former the granules are mostly yellow or brown, in the latter they are black (melanin). When the coloration of the skin is more marked, pigment is found in the other cellular layers of the rete. Among fibrous tissues the pia mater, the choroid, the sclerotic, and the cutis are the most frequently pigmented ; and brown or yellow granules are likewise found in the connective-tissue cells of the heart-muscle.

These pigmentations may become more marked under pathological conditions. Thus in Addison's disease, in the course of a general disorder leading to profound cachexia and associated as a rule with changes in the supra-renal bodies, the normal pigment of the skin increases and the consequent color-changes are very pronounced (*cutis æenea* or bronzing). So too in atrophic conditions of the heart, the normal pigment is markedly increased. In the voluntary muscles also, when they pass into atrophy, yellow pigment is frequently discoverable.

The highest degree of pathological pigmentation is met with in morbid new growths, such as tumors (nævi, melano-carcinomata, melano-sarcomata). The amount of pigment may become so great that the tissue looks uniformly and intensely black.

The pigment lies usually within the cells of the tissue, less often in the intercellular substance. In either case, as above remarked, it may take the form of yellow, brown, or even black granules ; or of diffuse staining of the protoplasm. Of its mode of formation we know nothing. It is possible that the coloring-matter is derived from the blood, but we are unable to determine in what way the derivation is effected.

[Laycock (*Medico-Chir. Review*, i., 1861) discusses and classifies the various forms of morbid pigmentation ; he gives full references to previous papers on the subject.

Gussenbauer has lately attempted ("Virch. Arch.," vol. lxiii.) to re-

fer the production of melanin in pigmented tumors to a modification of the coloring-matter of the blood. He thinks the blood-vessels of the tumor become here and there thrombosed; the coloring-matter of the blood escapes from them by diffusion, saturates the tissue, and is ultimately precipitated in granular form. Langhans ("Virch. Arch.," vol. xlix.) had previously sought to derive the pigment of tumors from cells containing blood-corpuscles (Art. 68).

According to Kunkel ("Sitzungsb. der phys. med. Gesell.," Würzburg, 1881), it is possible to isolate from melanotic tumors a pigment containing iron. This argues that the pigment is derived from the blood; but we cannot as yet say by what process it is produced. It is not related to hæmatin, bilirubin, or hydrobilirubin, as the spectroscope shows. It seems doubtful whether the escape of the coloring-matter from the blood-vessels always occurs in the way described by Gussenbauer. The diffused staining of individual cells may perhaps suggest that the coloring-matter first infiltrates the cell, and then breaks up into granules.]

68. **Hæmatogenous pigments** are such as are demonstrably derived from the coloring-matter of the blood. They generally originate in blood which has escaped from the vessels. More rarely the change to pigment occurs in blood which is still circulating. As is well known, the color-changes recognizable by the eye take place very quickly in small extravasations as well as large. In the skin, such extravasations become first brown, then blue, then green, then yellow. Where small hemorrhages have occurred in the deeper tissues, such as the peritoneum, pleura, or lungs, we find, even long afterward, brown, or gray, or black spots and patches. Larger hemorrhages (apoplexies) into the substance of the brain or lungs take on after a time a rusty brown color; and still later leave only a dirty yellow or yellowish brown staining. All these color-changes correspond to definite chemical and physical transformations of hæmoglobin.

Wherever in the tissues or in a cavity of the body a hemorrhage may have occurred, there ensues a series of changes in the escaped blood of which the following are the most important.

One part of the blood, including red cells as well as plasma, may be re-absorbed by the lymphatics and carried off unchanged.

Another portion of the corpuscles may become in a way dissolved; their hæmoglobin diffuses from them into the surrounding tissues, and the pale residual stroma breaks up and disappears. It is this diffused and altered coloring-matter (or hæmatin) which gives rise to the color-changes in cutaneous extravasations, as it passes through various transformations. The transformed pigments (which are similar to the biliary coloring-matters) are partially re-absorbed and at length excreted in the urine (urobilinuria); another part crystallizes in the tissues, and forms the orange or ruby-red rhombic tablets and needles known as hæmatoidin-crystals (Fig. 18, *B*). These are very frequently found as the residue

of old hemorrhages, such as occur in the brain; they may remain a long time in the tissues without change.

A third portion of the corpuscles shrink up or crumble down into brown granular masses. This is especially the case in the large extravasations forming so-called hæmatomata. These masses become in part transformed into brown amorphous pigment. This lies free in the tissues, and often becomes darker in color with age.

A fourth, and that the greater portion of the corpuscles and the products of their disintegration, is taken up by leucocytes (Art. 114), which gather in large numbers round the seat of extravasation and even penetrate into it. The cells become in this way corpuscle- and pigment-carriers (Fig. 18, *A*, *a* and *b*). The transformation of the hæmatin into

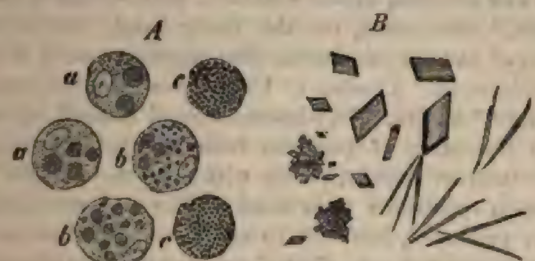

FIG. 18. × 500. *A*. Cells containing red Blood-corpuscles; in *a* the fragments are few but large, in *b* and *c* they are numerous and minute. *B*. Rhombic Tablets and Needles of Hæmatoidin.

brown pigment is completed within these cells, the corpuscles breaking up into minute granules (Fig. 18, *A*, *b* and *c*). The pigment may be set free again by the disintegration of the carrier-cells. Probably the cells have also the power of eliminating it, without themselves perishing.

These various modes of transformation of the blood-corpuscles very frequently go on at the same time in the same extravasation. Their ultimate result is, in the first instance, a local discoloration, due to pigment partly amorphous and partly crystalline in character. Secondary pigmentation of remote organs such as the lymphatic glands, the spleen, and the liver, may follow upon this, owing to absorption of the pigment by the lymphatics.

The formation of pigment in blood which is actually circulating is not carried beyond the first stage (the breaking up of the red corpuscles) within the vessels (Arts. 262 and 268); the completion of the process is effected outside the vessels. The pigments just described are only in part organic derivatives of the coloring matter of the blood (like hæmatin and hæmatoidin). A considerable part is composed of an inorganic iron-compound; namely, the hydrated sesquioxide (Kunkel). This is especially the case in large extravasations, where the hæmoglobin is decomposed on the spot. The contained iron being thereupon set free in the form of oxide, remains where it is and forms yellow or brownish flakes.

[It may be of use to mention that *hæmoglobin* is the unchanged coloring-matter of the blood as it exists in the living corpuscles. *Hæmatin* is the colored constituent obtained when hæmoglobin is decomposed (*e.g.*, by boiling); the other constituent being a proteid body. *Hæmatoidin* is formed when the decomposition is carried still further; it is identical with bilirubin (see Gamgee, "Physiol. Chem.," i., 2).

The first exact researches into the nature of the blood-pigments were made by Virchow ("Virch. Arch.," vols. i., ii., iv., and vi., and "Cellular Pathology"). He sought to show that hæmatoidin is to be regarded as the typical final resultant of the transformations of hæmoglobin within the human body. He assumed that the hæmoglobin escaped into the tissues unchanged, and was then, by a secondary process, transformed into granules and crystals, either within or without the cells. Langhans ("Virch. Arch.," vol. xlix.), on the other hand, maintained that the transformation of the red corpuscles into pigment could only take place inside the carrier-cells. Cordua ("Ueber den Resorptionsmechanismus von Blutergüssen," Berlin, 1877) has convinced himself by his investigations that the formation of pigment from hæmoglobin may take place partly outside the carrier-cells, partly within them. Ziegler's researches, carried out upon specimens from dead bodies and upon extravasations experimentally produced, lead him to agree with Virchow and Cordua.

Perls pointed out ("Virch. Arch.," vol. xxxix.) that the hæmatogenous pigments all yield the reaction of ferric oxide when treated with ferrocyanide of potassium and hydrochloric acid. Even when the pigment has become black it still exhibits the reaction. Kunkel was the first to show ("Virch. Arch.," vol. lxxxi., and "Zeitschr. f. phys. Chemie," iv., v.) that the brownish red flakes found in old extravasations are not always composed of hæmatoidin. Sometimes these flakes contain no organic coloring-matter at all, but consist entirely of hydrated ferric oxide. The urobilin (hydrobilirubin), which appears in the urine when free absorption of large extravasations takes place, is derived either directly from hæmoglobin, or from hæmatoidin. Further details on the disintegration of the blood under normal and pathological conditions, and the pigmentations connected therewith, are to be found in the Special Pathological Anatomy, Arts. 262 and 268.

A distinction must be made between the true slate-colored pigmentation of the tissues dependent on certain blood pigments, and the slaty discolorations seen in corpses (pseudo-melanosis), chiefly in the intestinal canal and its neighborhood. These discolorations, usually in the form of indefinite and diffused gray patches, are due to the formation of ferrous sulphide; combination takes place between the iron of the hæmoglobin present and the sulphuretted hydrogen evolved in commencing decomposition.]

69. **Biliary pigmentations.** If the excretion of bile be in any way hindered, it passes over into the general circulation, and biliary pigments

are thus carried to the various organs. The yellow staining of the tissues so brought about is called **icterus** or **jaundice**. When jaundice persists for some time the tint becomes olive-green or dirty grayish green. The bile in the tissues is usually diffused through them indefinitely; more rarely granules and ruby-red crystals occur. Crystals are chiefly found in the tissues in the so-called **icterus neonatorum,** or jaundice appearing within a few days of birth. These crystals take the form of ruby-red rhombic tablets, and are composed of bilirubin; they are identical with hæmatoidin-crystals. In the jaundice of adults crystals are seldom found; generally the pigment is more granular, and yellow or brown. This is especially the case when it occurs in the cells of the liver, and in the uriniferous tubules. In addition to the hepatogenous jaundice which depends on reabsorption of bile, there is said to occur also a hæmatogenous form resulting from a disintegration of blood within the blood-vessels; this is however disputed by many observers.

[The hypothesis of a hæmatogenous jaundice was based on certain experimental phenomena by Kühne ("Virch. Arch.," vol. xiv.). He injected dog's blood, in which the corpuscles had become dissolved, into the vessels, and then found bile-pigments in the urine. Kunkel ("Virch. Arch.," vol. lxxix.) questions the decisiveness of these experiments. Since bile-pigments are formed in the liver by the disintegration of red corpuscles, the process of pigment-formation would be intensified by Kühne's injections, and the surplus bile produced might in part pass into the blood again. Orth has a paper ("Virch. Arch.," vol. lxiii.) on the deposition of bilirubin-crystals in the jaundice of infants.

The most various theories have been started from time to time to account for *icterus neonatorum*. Birch-Hirschfeld has recently ("Virch. Arch.," vol. lxxxvii.) treated the question afresh. He maintains that the benign form of jaundice (*i.e.*, jaundice not depending on septic infection or profound anatomical change in the liver), is the result of œdema of the capsule of Glisson. This œdema arises in consequence of venous engorgement in the region of the remnant of the umbilical vein and vena portæ. This explanation seems somewhat far-fetched. May not the jaundice simply depend on an overgreat resorption of bile from the meconium?]

70. **Pigmentation** of the tissues **by extraneous substances.** Any substance optically distinguishable from a tissue, which becomes in any way incorporated with it and remains for a time unchanged, may give rise to a special coloration of the tissue. The number of such substances is of course large, and the manner of their incorporation various. The commonest avenues of entrance are surface-wounds, the air-passages, and the alimentary canal.

The most familiar instance of wound-staining is **tattooing**, common among civilized peoples as well as among savages. The way in which

the colored tattoo-marks are produced is this : the skin is first wounded by scratches or punctures, and then insoluble granular coloring-matters, such as charcoal, cinnabar, etc., are well rubbed in. Where the skin is broken the colored particles penetrate and infiltrate the cutaneous tissues. One part remains where it is, so that the skin continues permanently pigmented ; another part is carried off to the lymphatic glands, which also become pigmented.

The lungs and their lymphatic glands may become very deeply pigmented by the long-continued inhalation of foreign matters, such as coal-dust, soot, particles of iron or rust, etc. In consequence of prolonged inhalation of coal-dust, for example, the lung-tissue may become perfectly black (**miner's lung**).

Among the pigmentations arising from matters taken up in the alimentary canal, we must mention the so-called **argyrism** (*argyria*). This is a staining of the tissues consequent upon long-continued internal use of salts of silver. The skin in such cases may assume an intense brownish-gray color ; and the internal organs may also be more or less discolored. The silver is deposited as fine granules in the ground-substance of the different tissues.

CHAPTER XVII.

THE FORMATION OF CYSTS.

71. A **cyst** is an excavation bounded by an envelope of fibrous tissue or other more complex structure, and enclosing contents distinguishable from the envelope. According to its mode of origin the inner surface of the envelope may be lined with epithelium or with endothelium.

Epithelial cysts arise by the dilatation of pre-existing epithelial cavities. The commonest instance of this is the glandular cyst, which ensues upon closure of the gland-duct. The secretion collects behind the obstruction, and the gland dilates to a cyst filled with altered secretion. **Cysts of retention**, as these are called, are chiefly met with in the uterus, intestine, mamma, kidney, and skin.

In the case of ductless organs, like the Graafian follicles and the thyroid, dilatation of the cavities ensues whenever the secretion is morbidly increased. Cysts may also be formed in glandular structures occurring in morbid new growths. Various canals, moreover, which are normally clothed with epithelium, may, in consequence of obstruction and local dilatation, develop into epithelial cysts. Such canals are, for example, the bile-duct, congenital cervical fistulæ, the vermiform appendix, and the ureter.

Endothelial cysts arise primarily by dilatation of pre-existing cavities in the connective tissues, such as bursæ, tendon-sheaths, obstructed lymphatics, etc. In other cases they are owing to the collection of fluid in new-formed or false membranes. The contents of these cysts vary with their mode of origin, but consist generally of mere lymph. These might also be described as cysts of retention, in a special sense of the term; they are really exudation-cysts.

The cavities which are formed in the substance of a solid organ by softening and disintegration of a defined region are very frequently described as cysts. Such cysts occur, for example, in the brain, and they usually contain semi-liquid detritus of the brain-substance. Similar cavities arising in tumors by the same process are also called cysts. In order to emphasize the difference between such cysts and cysts of retention, the former may be spoken of as **cysts of disintegration**.

Lastly, a species of cyst may be formed around a foreign body which has become lodged in the tissues; round a parasite like a hydatid, for

example (Art. 245). It is the result of a new tissue-formation in the neighborhood of the foreign body.

[The student should consult the admirable lectúres on "Cysts" in Paget's "Surgical Pathology;" they contain many references of value.

To the varieties in the text we might add—**cysts of extravasation**, or blood-cysts, resulting from hemorrhage into closed cavities (*e.g.*, hæmatoma, hæmatocele); and **dermoid cysts**, which are congenital (Art. 178). The various neoplastic cysts or cystoid tumors will be referred to under their proper headings in Section VI.; and, so far as they affect particular organs, in the Special Pathological Anatomy.]

SECTION IV.

PROGRESSIVE OR FORMATIVE DISTURBANCES OF NUTRITION.

CHAPTER XVIII.

THE CELLULAR PROCESSES CONCERNED IN HYPERTROPHY, HYPERPLASIA, AND REGENERATION.

72. In treating of the malformations, we had occasion to speak of excessive development of the organism as a whole, and of its constituent parts—of over-size and over-growth. When a tissue manifests an abnormal tendency to overgrowth, it is said to **hypertrophy.** This term tacitly implies that the structure of the overgrown tissue continues to correspond with that of the normal.

The overgrowth first described implies an excessive development of the organism, or organ, in the embryonic stage of existence. Such forms of overgrowth form, however, but a part of the class of tissue-changes described as hypertrophies. In adult life, as in infancy, certain organs are very apt to hypertrophy, that is to increase abnormally in size while preserving their normal structure. Such hypertrophies are to be met with in the voluntary muscles, the heart-muscle, the unstriped muscles of the alimentary canal, bladder, and ureters, in the kidneys, thyroid gland, skin, etc.

The increased size of a hypertrophied organ depends on two factors. The several elements of the organ may increase in size, or they may increase in number. With Virchow we may distinguish between **simple hypertrophy,** *i.e.*, elementary overgrowth in the stricter sense of the term, and **numerical hypertrophy** or **hyperplasia,** *i.e.*, an increase in the number of constituent cells or cellular structures in the organ or tissue. Thus a muscle may very greatly increase in bulk by mere increase in size of each fibre of it; while the number of fibres remains the same. Of course, hypertrophy and hyperplasia may go hand in hand in the same tissue; indeed it is hard to conceive of a hyperplasia which has not been preceded by a hypertrophy, at least of some of the cells.

When an increase in the number of cellular elements occurs at a part where tissue has already been destroyed by some retrogressive process, we speak of it as **regeneration.** We assume that the formation of new tissue does not go on beyond the normal limit, but suffices merely to replace what has been lost.

73. Hypertrophy, hyperplasia, and regeneration are dependent ultimately upon certain cellular processes. The formation of new tissue can

only take place through the agency of the cells. The intercellular substance, unaided by the cells themselves, has no power or potency to produce new tissue. The cells which go to form new tissue arise by subdivision from pre-existing cells. New cells are never generated from plastic exudations, as was formerly supposed.

Hypertrophy, *i.e.*, increased size of a cell, is in general consistent with the maintenance of the properties of the cell. The formative process which results in hypertrophy is confined to the addition of new constituents similar in kind to those already present; the cell simply grows. We know but little of the structural changes which this growth involves. It is, however, sometimes noticed that the cell-protoplasm becomes more granular; or that the granulation alters as its amount increases; the nucleus also changes more or less its appearance.

Our knowledge concerning the process of cell-multiplication, or **proliferation** (as it is called, though the term is not a happy one), is more minute. Researches, most of them very recent, have shown that multiplication is attended by peculiar changes in the structure of the cell and of its nucleus, which affect the disposition of their several constituents. Movements within the nucleus are usually the first sign that cell-division is about to take place. These issue in subdivision of the nucleus. Then sooner or later the protoplasm as a whole is set in motion, and this ends in the complete subdivision of the cell itself.

74. The fully developed nucleus of a cell is not homogeneous, but possesses a very peculiar structure. This is clearly to be made out, by appropriate handling, under the higher powers of the microscope. A resting nucleus, *i.e.*, one which is not about to subdivide, consists of an external capsule or membrane (Flemming, "Virch. Arch.," vol. lxxvii.), and certain contents. The latter are divisible into a denser highly refractive nuclear substance, and a rarer colorless nuclear juice, or intermediate substance. The nuclear substance contains—first, certain nucleoli or nucleolar corpuscles, and secondly, scattered granules and filaments. Frequently the filaments are aggregated into a framework or network (Fig. 19, *a*), which may be brought out very distinctly by proper reagents.

When the cell is about to subdivide the nuclear network undergoes a series of typical changes of form, ending in the division of the nucleus into two equal portions.

According to Flemming, the first stage of **nucleus-division** is the solution and disappearance of the nucleoli; while the nuclear substance takes the form of a ravelled coil of sinuous filaments (Fig. 19, *b*); this is the "coil-form" of the mother-nucleus. The nuclear membrane itself seems to break up and furnish filaments to the coil. From this stage onward the nuclear figure alone takes up the staining reagent (hence the nuclear substance is sometimes spoken of as chromatin).

The filaments then become thicker and the coil looser; its continuity is broken here and there, and at length it passes into the "wreath-form"

(*c*). In this the filaments are arranged in a loose series of central and peripheral loopings, the centre of the figure being unoccupied. From this is fashioned a "star-form," or *aster* (*d*), with free double rays, the peripheral loops of the wreath-form dividing at their ends. The double rays next divide longitudinally, and the whole star-form contracts. The filaments of the single-rayed star (*e*) thus formed next gather into an equatorial group, which soon divides into two equal polar segments (*f*). This division is effected by the development of a transparent equatorial plate (*g*) often studded with fine points (Strasburger's cell-plate). The two segments, which are the rudiments of the daughter-nuclei, move

FIG. 19.—Indirect Cell-division (from Flemming; diagrammatic). *a*, cell with resting nucleus; *b*, coil form of mother-nucleus; *c*, wreath-form showing the central and peripheral loops, some of them broken through; *d*, star-form with free rays, showing the filaments in the act of splitting; *e*, fine-rayed star-form; *f*, nucleus with equatorial plate; division into polar segments; *g*, half-barrel or half-spindle form; the points in the middle are Strasburger's equatorial cell-plate; *h*, star-form of daughter-nucleus; *i*, wreath-form; *k*, coil-form; *l*, resting nucleus with network.

asunder toward opposite poles and form the "half-barrel" or "half-spindle" figure (Eberth's and Maizel's "creel-form," or "basket-form"). The half-spindle form of the daughter-nucleus passes into a star-form (*h*), and this into a wreath-form (*i*) by the fusion of the ray-ends. The wreath-form shrinks and its filaments become more ravelled, till at length it takes the coil-form (*k*). This becomes looser and more regular, and so finally the daughter-nucleus fashions itself a nuclear network (*l*), and passes into the resting state corresponding to the resting state of the mother-nucleus.

In the stage of the star-form and the wreath-form of the daughter-nucleus, constriction of the cell-protoplasm commences (*i*), and ends with the completion of the coil-form (*k*). During the active stages of the subdividing process the nuclear juice or intermediate substance does not stain, though it stains in the resting state. During subdivision the nucleus is surrounded by a clear areola. The whole process takes place rapidly; it ends with the complete constriction and severance of the cell-proto-

plasm. The above mode of subdivision is called indirect or **karyokinetic** (καρυον, a kernel).

[According to a recent communication of Flemming's ("Arch. f. mikrosk. Anat.," xx.), the intermediate substance of the nucleus contains (in stained preparations, and presumably also in the living state) a delicate prolongation or continuation of the nuclear network. The fine granulation observed in the intermediate substance with lower magnifying powers is really but an optical section of the meshes and filaments of the finer network. The nuclear membrane is merely the peripheral expansion of the nuclear network.

Most important and valuable researches on the changes in cells and nuclei during subdivision have been made by Flemming ("Arch. f. mikrosk. Anat.," xvi.–xx.) and Strasburger ("Zellbildung und Zelltheilung," Jena, 1880). The former has worked upon animal cells, the latter upon vegetable cells. Strasburger's description of the process of nucleus division is not quite the same as Flemming's. He distinguishes a nuclear substance (chromatin), and a nuclear juice (achromatin). The capsule or nuclear membrane, as well as the granules, network, and nucleoli which lie in the interior, belong to the nuclear substance. When the nucleus sets about subdividing, its granulation becomes coarser, and the granules run together into convoluted filaments; the nucleolar corpuscles and capsule also take part in forming the filaments. These filaments have the power of stretching or streaming out into the cell-protoplasm. Then follows an elongation of the nucleus and, at the same time, of the filaments, so that the whole assumes a spindle-like shape, and two poles become distinguishable. The filaments shrink up toward the equator, and so form the nuclear disc, the entire nuclear substance going to make it. From this account it appears that the nuclear disc consists entirely of shortened rodlets or filaments. On both sides of this equatorial disc appear slender striæ or filaments, the so-called spindle-filaments, and these together with the nuclear disc make up a secondary spindle-form of which the disc constitutes the equatorial zone. The spindle-filaments converge at the poles, or end freely. The material of which they are made is furnished by the cell-protoplasm. They are not taken up by the nuclear substance; indeed they are eliminated again as the subdivision proceeds. The daughter-nuclei originate in the nuclear disc. This parts asunder at the equator, and the two halves draw apart toward the poles. These halves become the daughter-nuclei; they are still connected by a few fine spindle-filaments. A row of granules now makes its appearance in the equatorial plane; this is the cell-plate, and in this the new cell-wall is formed. Protoplasm appears on each side of it, in which the spindle-filaments are merged—and thus the process of division is completed.

Strasburger's account of cell-division in the vegetable kingdom would seem to indicate that a certain difference exists between that and the animal kingdom. Flemming, however, has shown in a recent paper that the

physical processes involved in karyokinetic subdivision are in all cases essentially the same, at least in so far as they are to be made out optically. He thinks the apparent differences are not so great as Strasburger conceives them to be.

It is of great interest to note the fact established by Flemming—that in the segmentation of the ovum the process of nucleus-division follows throughout that which we have described as the karyokinetic mode (Balfour, "Comp. Embryology," i., 3).

This mode of nucleus-division has often been observed and described as occurring in pathological proliferations. The chief memoirs are by Eberth ("Virch. Arch.," vol. lxvii.), Arnold ("Virch. Arch.," vols. lxxvii., lxxviii.), Flemming (*loc. cit.*), Martin ("Virchow's Archiv," vol. lxxxvi.), Drasch ("Wiener Sitzungsber.," 1881), Klein (*Quart. Journ. of Micr. Science*, 1878 and 1879). Priestley gives a summary of the early researches in *Quart. Journ. of Micr. Science*, 1876 ; Cunningham reviews the more recent ones in the same journal, January, 1882.]

75. These structural changes in the nucleus point unmistakably to the energetic internal motions which affect its molecules in the process of growth. Our knowledge of the molecular changes in the cell-protoplasm is unfortunately more meagre and incomplete. Here, however, it is also possible to make out by proper means—that the protoplasm assumes a special structure, and that various movements and transmutations of form occur amongst its component elements. Thus in certain cases nucleus-division is accompanied by lively rotary movements in the protoplasm. Such transformations and transpositions explain certain phenomena which are frequently observed—for example, the formation of a transparent areola round the subdividing nucleus, of radiating lines of granules making up the so-called "karyolytic" figure, etc. Such radiating lines of granules have especially been seen in the process of impregnation of the ovum. They occur in the neighborhood of the male and female pronuclei, and have been described as the *aster* (Balfour, "Comp. Embryology," vol. i., ch. 3). Flemming, as well as Strasburger, assigns to the cell-protoplasm an essential part in the process of subdivision. Strasburger even asserts that it is the penetration of the protoplasm into the nucleus which calls forth a reciprocal activity in the latter, and so gives it an impulse toward subdivision. Whether this be true or not we cannot at present decide, inasmuch as no penetration of the protoplasm into the nucleus has ever been directly observed. The ordering of the granules into radiate figures, like the other movements of the protoplasm hitherto observed, takes place, as a rule, simultaneously with the process of nucleus-division. In some cases, however, it may precede, in others it may succeed, the latter. Thus, according to Gruber ("Zool. Anzeiger," 1880) the infusorian *Euglypha alveolata* first gives rise to a daughter-cell, then the nucleus becomes subdivided and migrates into the daughter-cell ; while at the same time active movements become visible in the cell-protoplasm.

A special form of cell-division is that which takes place after an antecedent conjugation. It is common among the infusorians.

[In order to make out the nuclear figures, the cell must be examined either in the living state or after treatment while still living with a rapidly fixing solution. If this is not done the process of subdivision is completed as the cell gradually dies. There is no general rule of proceeding which will apply to the examination of all cells.]

76. The indirect process of cell-division just described will serve as a pattern of the processes which occur in pathological cell-formation. No satisfactory demonstration has been given of the theory that cell-division may occur in another way, namely by direct constriction of the cell without interior structural change. Nor has it been certainly established that a nucleus or cell can arise *de novo* out of an indifferent blastema (or homogeneous matrix), at any rate within the domain of pathological cell-formation. Virchow's aphorism, *Omnis cellula e cellulâ*, is, in this domain at least, most fully and completely confirmed.

But though we maintain that, so far as we know, cell-division is always indirect, never direct, we do not imply that every cell-division proceeds exactly according to the scheme we have indicated. On the contrary, the examination of different specimens shows that the form and construction of the nuclear figures are by no means always the same; deviations within certain limits may occur.

But while the figures formed by the nuclear filaments may differ considerably, the principle and plan of the process is fundamentally the same. Even the simultaneous formation and development of three or four daughter-nuclei is but a modificatien of the general process.

The subdivision of the cell-protoplasm usually follows immediately upon the division of the nucleus; but the connection of the two processes is by no means inevitable. Not infrequently the nucleus subdivides while the cell does not. The result is the formation of binucleated, or finally of multinucleated cells, the so-called **giant-cells**. These giant-cells may afterward break up into uninucleated cells, the protoplasm gathering itself around the several nuclei and dividing along the boundaries of the regions so defined. Sometimes this happens in a peculiar way. The protoplasm of the daughter-cell separates from that of the mother-cell, but in such wise that it remains surrounded by the latter on all sides; the one cell includes the other. Virchow has called such cells **brood-cells**. They do not occur frequently. They have been thought commoner than they really are—inasmuch as leucocytes which have penetrated into a large ordinary cell have been taken for a brood of daughter-cells. The process of cell-division takes a peculiar form also in the formation of cell-buds, or **gemmation**. The mother-cell shoots out a longer or shorter process; this then receives a nucleus; and lastly divides off from the parent (see under New Blood-vessels, Art. 86). The

peculiarity is chiefly in this—that the movements of the protoplasm (evidenced by the protrusion of the bud) precede the nucleus-division. The new nucleus, derived, as in all other cases, by subdivision from the mother-nucleus, migrates into the bud after it is already marked off from the parent.

[Until quite lately the process of nucleus-division was described (after Remak) somewhat in this fashion: The nucleus lengthens out, becomes indented and constricted in the middle, and at last divides (compare Rindfleisch, "Pathological Histology," vol. i., p. 71; Cornil and Ranvier, "Manual of Path. Hist.," vol. i., pp. 9, 83). The constricted bean-shaped nuclei found in some preparations were regarded as in the preliminary stages of subdivision; and the multiplication of the nucleoli was regarded as the first step in the actual process. This view must now be given up. The various shapes of the nuclei depend partly on actual contractions, partly on shrinkage during the hardening process. Increased size of the nucleus may perhaps have a relation to its imminent subdivision; the mere multiplication of its nucleoli has certainly no such relation.

The older theories of direct nucleus-division have been discredited by the latest researches; so also have the still older views concerning the formation *de novo* of cells and nuclei. (See Strasburger, *op. cit.*, where full references to the literature of this subject are given.)

The question whether or not the white blood-cells subdivide is as yet unsettled. Indirect nucleus-division has not been observed in them. See Klein, "Centralb. med. Wiss.," 1869, *Quart. Jour. of Mic. Sci.*, 1875, and "Handb. of Phys. Lab.;" Ranvier, "Traité technique d'histologie," p. 161.

On "endogenous gemmation," by which brood-cells are produced, see Virchow, "Cellular Pathology," and Klein, "Wiener Sitzungsber.," 1871, and "Anatomy of Lymphatic System," vol. i., London, 1875.]

77. The formation of new cells is the first step toward hyperplasia as well as toward regeneration. They yield the formative tissue out of which the definitive structures are developed. As the processes of cell-division in pathological new-formations are closely analogous with those of normal multiplication, so also do the succeeding formative processes run parallel with those of normal growth. If epithelium or fibrous tissue is to be fashioned out of the indifferent tissue which results from cell-division, the process of transformation is exactly the same as occurs in the normal development of the organism from embryonic tissue.

So far as investigation in this region has yet extended, we find the law of the **specific nature of the tissues** to be everywhere obeyed. The cell-progeny of the embryonic cells which went to form any given layer of the blastoderm can go to build up such tissues only as are normally derived from that layer. An epithelial cell can in no possible circumstances form bone or cartilage; a connective-tissue corpuscle cannot bring forth an epithelial cell or a gland-cell. This law has frequently been called in question; the specific distinction between the various tissues was for-

merly not recognized or not accepted. Thus Virchow, to whom we owe the fundamental principles of cellular pathology as regards new-formations, held that connective tissue might serve for the matrix of the most various structures. This view is no longer tenable ; observed facts constrain us to believe that a tissue cannot give rise to new tissue other than of its own kind or kindred.

Epithelial tissues are, generally speaking, built up by the cementing together of formative cells in a way which is characteristic of epithelium everywhere ; the cells are in juxtaposition, the intercellular cementing substance is subordinate. In fibrous tissue, on the other hand, the intercellular material derived from the cells is the chief constituent, and gives to the tissue its characteristic properties.

78. A morbid growth is the product of various factors. If a cell is to grow and multiply it must first be endowed with the faculties necessary to growth and reproduction. In other words, it must have the power to take up from the blood a greater quantity of nutriment, to assimilate this, and apply it to the formation of new protoplasm. This property of the cell Virchow has called the nutritive and formative excitability (*Irritabilität*); a term which implies that it is some stimulus or excitation from without which stirs up the cell to increased assimilation.

We must, therefore, begin by inquiring of what kind the stimuli must be that can thus excite the cell to intenser activity.

When, in embryonic development, a part or organ grows to an abnormal size and thus becomes so to speak gigantic, we may refer the phenomenon to several possible originating causes. The primary rudiment of the part may have been unusually large ; the embryonic cells may have been endowed with an abnormal share of vital energy ; they may have had specially favorable chances of nutrition ; the resistances to proliferation may have been abnormally slight. It is not, in general, an easy task to decide which of these factors has in a given case determined the result. It is, of course, always possible that several factors have been working together.

In the hypertrophies of later life (including the hyperplasias and regenerations), which are demonstrably conditioned from without, and so do not depend on pre-existing or embryonic factors, the question of etiology is so far simplified. We must direct our attention to the other possible factors, namely increased vital energy, increased supply of nutriment, or diminished resistance to growth. It is, however, not to be forgotten—that the cause of the increased activity of the cell may be of the nature of a stimulus from without, which acting directly upon the cell excites it to more intense productiveness. We may assert then in general terms that, when the nutritive and formative activities of a cell are morbidly increased, the effect is due to augmentation of the physiological stimuli or diminution of the physiological resistances to growth, or to the direct influence of external stimuli.

79. Experience has shown that many tissue-cells, even when they

seem, by their close connection with their neighbors, to be as it were firmly built into the tissue of which they form a part, still retain for a time the power of growth and subdivision, or, in other words, of multiplication. This is especially the case with cells whose protoplasm has not undergone any serious metamorphosis. As to the conditions governing such multiplication, experience alone can inform us.

Many observers (Stricker, Boettcher, Neumann, etc.) assert that extrinsic stimuli, that is to say physically or chemically active substances, have the power of exciting the cell to proliferate. Thus caustics and the actual cautery applied to tissues are said to induce in them cell-multiplication by direct action. There seems to be no certain observation which either establishes or confirms the assertion. Researches made in this direction have shown that the action of such external agencies is in the first instance destructive ; that in caustic corrosion, for example, not only does the tissue which is directly attacked perish, but that in its neighborhood undergoes secondary degeneration as well. It has furthermore been uniformly observed that formative changes do not begin to appear until a certain time after the injury ; it is therefore very unlikely that they are directly brought about by it. Lastly, they do not commence at the injured spot, but in its neighborhood.

From these considerations it appears that the proposition, often enunciated as if it were self-evident—"The stronger the external stimulus, the greater the proliferation"—cannot be accepted as true. We can at most admit that very slight stimuli, sufficient merely to excite the cell without injuring it, may perhaps call into play its power of multiplication ; but nothing has been experimentally established concerning the nature, the action, or the mode of application, of such stimuli.

[The researches on the reaction of cells to external stimuli have been made chiefly with the view of determining the source of the migratory cells in inflammation (Art. 99). Stricker and his pupils affirm that the stimulus of inflammation excites the affected cells to rapid multiplication. The tissue-cells and their appendages swell up (it is said) under this excitation, and subdivide into new cells and non-nucleated lumps of protoplasm (Stricker's "Vorles. über allg. Pathol.," Vienna, 1878 ; and "Pathology of Inflam.:" "Internat. Encyclop. of Surgery," vol. i., 1882). Cohnheim ("Lehrb. d. allg. Pathol."), Key, Retzius, Eberth, and others have failed to make out any such consequence of inflammatory irritation.

Even if the meaning of the word *stimulus* be extended to include any mechanical or chemical agency which can influence the cell, we cannot adduce any undoubted observation serving to establish Stricker's view.]

80. If, then, it be true that external injurious agencies are not competent to induce multiplication in cells, we must have recourse to the normal vital stimuli if we are to explain the process of pathological cell-

growth. For the due growth and multiplication of a cell certain external conditions must be fulfilled. Above all it is necessary to provide for a certain degree of warmth, and a certain modicum of proper nutritive material. In addition to this there must be no obstacle in the way of multiplication. These are the external requirements. The internal condition is the inherent faculty of the cell to assimilate the nutriment offered to it.

In a tissue not undergoing transformation, the factors favoring proliferation and those which inhibit it must be in a state of balance. If this balance be disturbed toward the side of the proliferous forces, the cells proceed to grow and to multiply. The factors in question resolve themselves on analysis into three.

In the first place, it is conceivable that the capacity of the cell to assimilate nutriment may be increased. Such increase can only be conditioned by an increase in the normal stimuli required for the preservation of the cell. Such stimuli are warmth, for many cells light, for the muscles motor impulses, for glands special excitations from the nervous system, etc. Increased stimulation of this kind may as a fact lead not only to intensified functional metabolism in the tissue concerned, but even to hypertrophy of its elements. Such hypertrophies, which we may call functional hypertrophies or hypertrophies of action, are specially common and remarkable in muscles and glands (heart-muscles, bladder-muscles, kidneys, etc.). As we have said, they are referable in part at least to increased vital activity in the cells, consequent upon increased physiological stimulation.

A second possible factor is increase in the supply of nutriment. This plays a chief part in hyperplastic processes, at any rate.

A third is the removal of the normal checks to growth. Its effect is most evident in the processes described as regenerative.

If we attempt in particular cases to make out to which of these factors cell-multiplication is due, we are led to see that it is rare for any one factor alone to be the efficient cause. The remarkable regulating mechanism of the vessels is so adjusted, that when the function of a tissue is increased its blood-supply is increased to correspond. In like manner, when the smallest fragment of tissue is removed, the slight loosening of the surrounding texture is enough to augment the stream of transudation from the vessels. In consequence of these adjustments, increased supply of nutriment plays a great part in all the formative disturbances of nutrition.

[Cohnheim, in his "Allgemeine Pathologie," has insisted on the importance of increased supply of nutriment even more strongly than we have done. According to his view it is the sole influential factor, compared with which the intrinsic activity of the cell is quite secondary. We are unwilling to condemn the cell to play so passive a part, but rather agree with Virchow, who ("Cellular Pathology") lays it down that

—"the cell is not nourished, but nourishes itself." Functional hypertrophy is therefore not to be looked upon as the mere consequence of the increased blood-supply to the active organ. If the assimilative activity of the cells were not augmented, the mere presence of a greater supply of nutriment would be valueless. See Samuel's "Allg. Path.," 1879; Paget's "Surgical Pathology," Lect. 3.]

81. We shall more readily comprehend the activity of the tissue-cells, *i.e.*, their behavior under various conditions, and the changes they pass through—now at rest, and now manifesting intense formative energy—if we consider first the vital manifestations of an organism that is unicellular. In later chapters we shall have frequently to speak of unicellular micro-organisms, of bacteria and yeast-plants, and their mode of life. If we reflect on the conditions essential for the multiplication of such organisms, we note that the nature of the nutrient fluid is (next after the adjustment of the temperature) the factor of highest importance. In suitably composed fluids the fungi develop much more luxuriantly than in those that are ill-suited. But we are not thereby justified in assuming that the cell plays a merely passive part, that all it has to do is to take up the nutriment offered to it. The cell is, on the contrary, active, and its activity has a special influence on the liquid itself. It has the power to induce certain chemical changes in the liquid, to decompose certain substances contained in it, and to change their condition so as to adapt them for assimilation by itself. The cell does not merely take in and give out material; it acts "catalytically" on its environment. This is proof at least that the cell possesses a high degree of spontaneity—that it has the power of making more available for its own sustenance the various forms of nutriment that come in its way.

It is also of great interest to remark that the cell is ultimately limited in its formative activity by its own products. When the amount of nutriment present is abundant, the activity of the cell comes to an end, not through the exhaustion of the supply, but through its contamination with certain products of cell-metabolism. Many of the substances engendered in fermenting liquids by the action of fungi tend to check the growth and multiplication of the fungi themselves; when present in quantity they may put a stop to multiplication altogether. The alcoholic fermentation, and the multiplication of the yeast-plant which produces it, come to an end when a certain proportion of alcohol has been generated in the fermenting liquid. In septic putrefaction the bacteria generate compounds, such as carbolic acid, which are destructive to themselves. If we may apply these facts of fungus-physiology to the cell-physiology of higher organisms, we find that they illustrate first of all this principle—that the quantity and quality of the nutritive material at the disposal of the cell have a profound influence upon its behavior. And secondly, this other—that the cell has nevertheless an intrinsic power of utilizing this material, and of appropriating what is suitable to itself out of various

combinations. Lastly, the limits imposed on the multiplication of fungi by the products of their own activity may help us to understand how the formative activity of the cells of complex organisms may be temporarily checked. We cannot indeed regard the intercellular substance of the connective tissues as equivalent in significance to the products of the chemical changes induced by the bacteria. Yet the comparison may at least enable us to conceive how cell-growth may tend to limit and to check itself, without the interposition of extrinsic resistances. In the connective tissues the formation of the intercellular substance is the limiting factor, in the epithelia it is the cohesion or cementation of the individual cells into a firm and single whole ; just as in yeast-fermentation it is the formation of alcohol. When the alcohol is withdrawn in the latter case the multiplication of the yeast-fungus goes on again. So, likewise, if the intercellular substance be dissolved away from a connective tissue, or if the continuity of the epithelial mosaic be loosened or interrupted, the faculty of multiplication is again awakened in the constituent cells ; or if (as in the epithelia) it has never been dormant, it is at once intensified.

[In the human organism temperature is not a factor of such importance as it is in regard to unicellular organisms. In the former the temperature is approximately uniform ; change of temperature cannot therefore play any great part in promoting cell-growth. Even changes in the quality of the cell-nutriment can have but a small part of the significance here that it has in the case of fungi living in a nutrient solution ; such grave changes as may be artificially produced in the character of the solution do not occur in the body. Quantitative variations are thus of the greater importance.]

82. It often happens in an organ which is the seat of hyperplastic proliferation that the different elements do not take an equal share in the process. Thus an enlarged gland may in one case owe its increase in size entirely to additions of gland-substance, in another to increase in the fibrous constituents. We may have a glandular hyperplasia, or a fibrous hyperplasia. This may happen in any organ which is composed of more than one kind of tissue. The inequality in the relation of the two tissues may be so extreme, that while one is highly hyperplastic the other may not merely fail to increase, but may even undergo atrophy. In the latter case it is generally the specific elements (ganglion-cells, nerves, gland-cells, muscles, etc.) which atrophy, while the fibrous elements increase and multiply. A very frequent cause of such unsymmetrical hyperplasia of the fibrous tissue is inflammation (which see). Inflammation plays a chief part in pathology ; only too frequently its disastrous result is **fibrous hyperplasia** of the affected organs, involving atrophy of their essential elements.

What is true of hyperplasia holds also for regeneration. When part

of a tissue has been destroyed, the regeneration which ensues is by no means always complete and perfect. In the human organism at least, the power of restoring or regenerating a lost part is very limited. Parts of any appreciable size when once lost are never replaced. This is true, for example, of a limb, a finger, a piece of liver, or of brain-substance. All highly specialized structures, and their specific elements, show but slight traces of regenerative power. Thus in adults it is highly probable that ganglion-cells are never reproduced, if once destroyed. Glandular epithelium is only restored when the loss is very trifling, and when some of the essential cells still remain intact within the gland-unit (acinus or tubule). When a gland is wounded and its texture broken into ever so little, the wound in healing fills up not with gland-substance, but with fibrous tissue. Pathological vicarious tissue of this kind is described as **cicatricial** or **scar tissue.** It is the result of an inflammatory process (Art. 108), or of multiplication among the connective-tissue cells.

With nerves and muscles the case is much the same. Deficiencies of any size are filled up with scar-tissue.

The connective and epithelial tissues are more favorably circumstanced. The latter especially have the power of reproducing wide areas of lost surface. Among the fibrous tissues, the periosteum is remarkable for its regenerative power; while cartilage is replaced very imperfectly, if at all.

83. When, by a process of proliferation, a new tissue is produced whose elements are normal in type, though the type is not that of the matrix-tissue, we speak of the formation as a **heteroplasia**. In one sense a cicatrix in an organ like the liver is a heteroplasia, inasmuch as fibrous tissue replaces the proper liver-tissue. And even when the fibrous tissue of the cicatrix is compared with that of the liver, we must still regard the cicatrix as heteroplastic ; the characters of the two tissues are markedly different. This is true of fibrous hyperplasias in general, and in particular of those consequent on inflammation. Owing to the generic resemblance of the normal and pathological tissues, however, it is not usual to reckon these among the heteroplasias.

The special field of heteroplastic formations lies among the tumors or morbid growths. A tumor, in the limited sense of the term, is a formation of new tissue. It may resemble more or less the matrix-tissue from which it grows, but it always possesses certain characteristics which distinguish it from the surrounding structures, and which justify us in speaking of it as heteroplastic.

CHAPTER XIX.

HYPERPLASIA AND REGENERATION IN PARTICULAR TISSUES.

84. The morphological changes which take place in the hyperplasia and regeneration of the epithelia are comparatively simple.

Epithelium can arise only from epithelium ; the several varieties even do not usually pass into each other. Eberth's researches ("Virch. Arch.," vol. lxvii.) have shown that the nuclear transformations in epithelial cells during their reproduction are quite analogous to those figured in Flemming's scheme. The disappearance of the nucleoli and nuclear membrane, the formation of filaments, of two semi-spindle forms (or, as Eberth calls them, "creel-forms"), of star-forms, etc., are all observed in the epithelial cell, within a clear areola of cell-protoplasm. The star-forms likewise, as they move asunder poleward, become transformed into nuclear networks in the midst of the clear intermediate substance of the daughter-nuclei. Arnold describes ("Virch. Arch.," vol. lxxviii.) nuclear figures observed in tumor-cells, which in details seem rather to correspond with Strasburger's version of the phenomena. The subdivision of the cell-protoplasm occurs either during the later stages of nucleus-division, or after it is complete. In other cases processes are first thrown out by the subdividing epithelial cell, and into these daughter-nuclei then migrate. The budded processes become independent cells by separation from the mother-cell.

Small losses of lining epithelium are in general replaced quickly by means of regenerative multiplication. Glandular epithelium, like that of the kidney, may also be quickly reproduced when lost, provided only the structure of the basis-tissue (from which the cells derive their sustenance) is not altered or destroyed. Hyperplastic multiplication of epithelial cells is very common, especially in tumors.

Epithelial cells have also the power of remaining alive for a time when separated from their proper matrix. They may in this way be transferred from one basis-tissue to another. Thus epithelial cells from the skin of one person may be transplanted to the surface of a granulating wound in another, and there grow and multiply (Reverdin's skin-grafting). This is a simple and convincing proof of the independence or autonomy of the cell, and of the importance of its inherent powers in reference to its nutritive and formative activity.

[The regeneration of epithelium has of late years been made the subject of numerous researches. Most observers agree that epithelium can arise only from epithelium ; only a small number, like Burkhard (" Virch. Arch.," vol. xvii.), Cornil and Ranvier (" Man. Path. Hist.," vol. i.), and Rindfleish (" Gewebelehre," fourth edition, p. 128 ; " Pathological Histology," vol. i., p. 106) assert that epithelium may be formed from connective-tissue cells. No convincing proof of the assertion is alleged ; while the fact that cutaneous wounds begin to skin over only at spots where epidermal cells still remain tells strongly against it.

Arnold (" Virch. Arch.," vol. xlvi.) believes that in epithelial regeneration a plasma is effused into which nuclei subsequently migrate. Klebs (" Arch. f. exper. Path.," iii.), von Wyss (" Virch. Arch.," vol. lxix.), Cohnheim (" Virch. Arch.," vol. lxi.), and Eberth (*loc. cit.*) have failed to confirm this, but found on the other hand that regeneration was effected by subdivision of the old epithelial cells. Klebs observed in the young cells phenomena suggesting contractility and the power of locomotion ; Waldeyer has made a like observation in the case of epithelial tumor-cells. The first communication on epithelial transplantation and skin-grafting was made by Reverdin (Soc. de chirurgie, December 13, 1869 ; *Brit. Med. Journ.*, 2, 1870 ; " Arch. gén. de méd.," 1872. His method has since been extensively employed with a view to the speedier skinning over of wounded surfaces (" Int. Ency. of Surgery," vol. i.). Schweninger has shown (" Ueber Transplant. von Haaren," Munich, 1875) that the mere laying on of hairs, which have been plucked out with the outer root-sheath adhering, suffices to set up epithelial proliferation on granulating surfaces.

Griffine (" Virch. Jahresber.," 1876) has shown that, when ciliated cylindrical epithelium is lost, it is first replaced by ciliated squamous epithelium ; this is then gradually transformed into the cylindrical variety.]

85. New **fibrous tissue** is invariably developed from cells, and the process is the same as that by which normal fibrous tissue is formed. The formative cells have been named **fibroblasts**. They are derived by proliferation either from the stationary cells of the connective tissue, or from migratory leucocytes, *i.e.*, white blood-cells which have escaped from the vessels. The development of the latter will be treated when we discuss inflammatory new-formations.

Fibroblasts are cells with large vesicular nuclei and nucleoli, and are capable of active subdivision and multiplication. By proper handling it is possible to make out the nuclear figures, but the subject has not been sufficiently investigated to afford means for a detailed description of the process of subdivision. The cell-protoplasm is pale and highly granular ; the size of the cell varies, on the average it is about that of an ordinary squamous epithelial cell. They are often described as epithelioid cells. Not infrequently multinuclear cells are met with, the so-called giant-cells. The form of the fibroblasts is extremely variable. In the earlier stages

they are rounded, later on they become club-shaped, spindle-shaped, star-shaped; in short they assume every possible shape and form.

When they have accumulated in any spot and begin to address themselves to the formation of tissue, they become connected with each other by means of their processes and projections; or they arrange themselves in a compact mass of densely packed multiform cells.

The intercellular substance which gives the fibrous tissues their characteristic texture is derived from the cell-protoplasm. The ends and lateral borders of the cells become fibrillated; or the boundaries between the cells disappearing, a homogeneous mass of protoplasm is formed, and in this fibrils are afterward developed. A great many of the formative cells are used up in this way; some, however, retain their nucleus and a part of their protoplasm, and form the fixed connective-tissue corpuscles of the new tissue. (Cf. Art. 108.)

According to the greater or less compactness with which the formative cells are deposited and grouped, the new tissue is firm and dense, or loose and reticular. Fibrous tissue, rather than areolar, is that most commonly developed, especially as a consequence of inflammation. It may become hyperplastic, either by itself, or accompanied by hyperplasia of contiguous tissues such as the epithelia. In respect of the diffusion or extension of the hyperplastic process, it is of some importance to distinguish between diffuse or indefinite hyperplasia, and that which is limited to definite areas; the latter leads to tissue-formations which resemble tumors. (See under Tumors, Sect. VII.)

Adipose tissue is formed from normal or pathologically developed connective tissue, or from mucous tissue, by the deposition of fat in the interior of the cells.

Mucous tissue, characterized by the mucous consistence of its ground-substance, is generally derived from an existing tissue by metaplasia (Art. 90); it may also be formed from new proliferating cells.

Neuroglia is developed by the multiplication of the neuroglia-cells.

[The structure and development of the connective tissues, both normal and pathological, have been the subject of many researches. The origin of the ground-substance has given rise to controversy. Some consider it to arise outside the cells, others from within them. A third theory again, while admitting its external origin, supposes that the fibrils are produced in it by the formative power of the cell as if they were a kind of plastic secretion. The view of the text only applies to the formation of fibrous tissue from new-formed embryonic or indifferent tissue. It does not apply, for example, to the formation of fibrous tissue by metamorphosis of the basis-substance of a different tissue, such as bone (see under Metaplasia, Arts. 90–92). For further details the reader is referred to the following: Virchow ("Virch. Arch.," vol. xiii.), Neumann ("Arch. für Heilk.," 1869), Aufrecht ("Wiener med. Wochenschr.," 1868), Rindfleisch ("Pathological Histology," vol. i., p. 92), Ziegler

("Untersuch. über path. Bindegewebs-und Gefässneubildung"), Perls ("Handbuch d. allg. Path.," i.), Tillmanns ("Virch. Arch.," vol. lxxviii.).]

86. The formation of **new blood-vessels** plays a chief part in hyperplasias of every kind. Wherever fibrous tissue, bone-tissue, gland-tissue, or any other is produced in quantity, new blood-vessels must of necessity be developed. In no other way is it possible to keep the new-formed tissue adequately supplied with nutriment. For this reason new blood-vessels

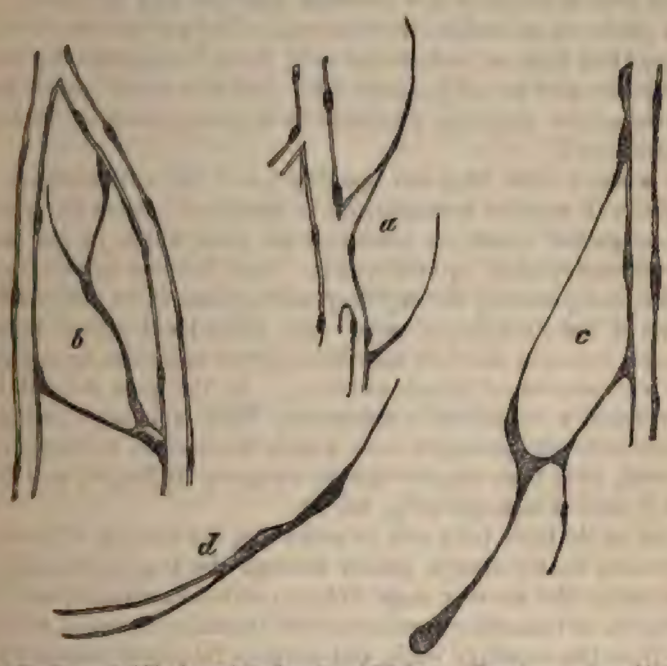

FIG. 20.—Development of Blood-vessels by Sprouts and Off shoots. (From preparations of inflammatory granulation-tissue.) *a, b, c, d*, various forms of vascular off-shoots; some solid (*b, c*), others in process of excavation (*a, b, d*); some single (*a, d*), others branched (*b, c*); some with nuclei (*b, c*), others without (*a, d*). Formative cells from without have attached themselves to the off-shoot *d*.

begin to be formed at a very early stage in all new growths, and they must be regarded as the chief factors in the formative process.

New blood-vessels are developed out of off-shoots which start from the walls of existing blood-vessels.

The first change observed is the formation of a conical sprout or projection on the outer surface of some capillary vessel. From the top of this runs off a fine filament of protoplasm, which gradually lengthens. The granular mass forming the projection increases in size, growing out into an irregular process or off-shoot. This is at first solid; but nuclei soon begin to appear among its granules. The off-shoot may become attached to another vessel; it may unite with a second off-shoot; or it may return back into the vessel from which it starts, forming an arch of

protoplasm (Fig. 20, *c*). From the solid off-shoot other secondary off-shoots may start (Fig. 20, *b*, *c*). Sometimes their extremities become club-shaped (*c*). The originally solid off-shoot becomes by and by excavated, by liquefaction of its central parts. The excavation quickly becomes continuous with the lumen of the vessel (*a*), or the wall of the latter bulges into the excavation. In either case the blood from the parent vessel penetrates the new one, and distends it. The excavation proceeds and extends onward to the point of junction of the new vessel with another, so that at length a new pervious capillary loop is formed.

The off-shoot, as it starts from the wall of the parent vessel, is in effect a sprouted bud from an endothelial cell; when it subsequently receives a nucleus it becomes an independent cell. The new blood-vessels are therefore intracellular channels, produced by the excavation of elongated or filamentous cells.

For a short time after the opening up of the new capillary channel the vessel-wall remains homogeneous in structure. Soon the protoplasm begins to gather round the nuclei of the wall, which in the meantime have been multiplying by subdivision. Cells become in this way distinguishable, and presently the capillary-wall appears in its perfected form as a mosaic of flat endothelial cells. (As Arnold and others showed, the boundaries between the cells may be rendered apparent by injecting the vessels with solution of nitrate of silver.) By this time the wall has generally reached a considerable thickness. This is in part owing to the fact that ordinary formative cells attach themselves in numbers to the vessel-wall; they then dispose themselves along its length, and thus tend to give it needed strength (Fig. 20, *d*).

So far as we have been able to make out, the process of forming new blood-vessels nearly always passes through the stages described. It is only at times that another stage is interpolated in which spindle-shaped, club-shaped, or branching formative cells become connected with the off-shoots from the capillary walls, and develop into new vessels by central excavation in the same way as the off-shoots themselves develop.

[The subject of the formation of new vessels has a special interest in reference to the theory of cell-multiplication. We have in this case to do not with symmetrical subdivision, but with gemmation; and moreover the initial movement is set up, not as usual in the nucleus, but in the cell-protoplasm. The protoplasm of the endothelial wall-cells throws out a non-nucleated process; the subdivision and migration of the nucleus is subsequent to the movement in the protoplasm.

The author has verified the above account in the course of his researches on granulation-tissue and on tumors (Ziegler, "Ueber path. Bindegewebs- und Gefässneubildung," Würzburg, 1876), Stricker ("Wiener Sitzungsberichte," 1865–1866), Golubew ("Arch. f. mikro. Anat.," 1869), and Arnold ("Virch. Arch.," vols. liii., liv.), have described the above mode of development of new vessels as observed in tadpoles' tails,

Travers in the foot-web of the frog ("On Inflammation," etc.). It is the only mode which certainly occurs in pathological formations. For this reason we have not given the customary enumeration of the primary, secondary, and tertiary modes formulated by Billroth ("Untersuch. ü. d. Entwig. d. Blutgef.," Berlin, 1856) and Rindfleisch ("Pathological Histology," vol. i., p. 89). In the primary mode the embryonic cells become directly transformed into red blood-cells on one hand, and into the parietal cells of a vessel on the other. The embryonic cells in fact arrange themselves into cords; the axial ones become blood-cells, the peripheral ones cohere as elements of the containing vessel-wall. This process takes place in the mesoblast of the embryo, but not in pathological formations (Klein, "Wiener Sitzungsberichte," 1871; *Quart. Jour. of Mic. Sci.*, 1872; Balfour, "Comp. Embryology," vol. ii.).

In the secondary mode (Billroth, O. Weber, Rindfleisch) spindle-shaped cells cohere to form cylinders in such wise as to enclose a continuous canal. This notion seems to rest on a mistake, occasioned by the fact that in granulation-tissue, for example, the vascular off-shoots are very quickly surrounded and wrapped about with spindle-shaped formative cells; and this gives the offshoots the appearance of strings of cells.

The so-called tertiary mode is that given in the text. Compare the description by Paget ("Surgical Path.," Lect. 10).]

87. Proliferation in **cartilage** may be either a regenerative or a hyperplastic process. The reproduction of cartilage-cells at the margin of a breach is effected by the cells first enlarging, and then undergoing subdivision of nucleus and protoplasm. Nuclear figures are observed. In this process many of the cells attain to great dimensions and may contain as many as twelve nuclei apiece (Ewetzky). The cells are rounded or branched, stellate or spinous. The capsular membranes disappear as the cells enlarge and multiply. Later on the cells or cell-groups become surrounded by the characteristic hyaline matrix-substance.

In hyperplastic proliferation the process is similar. The cells multiply and stretch the capsules, or cause them to give way and disappear; in like manner the intercellular matrix is distended or destroyed. Subsequently the new-formed cells generate for themselves fresh capsules and matrix-substance.

When a breach in cartilage is not repaired by multiplication of the cartilage-cells, fibrous tissue, developed from fibroblasts, usually fills up the gap. In other cases bony tissue is developed as well.

Cartilage may arise not only from cartilage, but from other allied tissues, such as growing periosteum in particular, perichondrium, marrow, bone, fibrous tissue, and epithelium. The metamorphosis is sometimes effected directly, as from perichondrium or marrow, sometimes through the intermediate stage of granulation. In the latter case an indifferent tissue is first formed, which is rich in single cells; these then become transformed into hyaline matrix-substance and cartilage-cells. Cartila-

ginous new growths are most commonly found in connection with the skeletal structures ; in other regions they are rare.

[Memoirs on the formation and proliferation of cartilage have been published by Virchow ("Onkologie," i.), Goodsir ("Anat. and Path. Obs.," 1845), Redfern (*Month. Journ. of Med. Science*, 1851), Ewetzky ("Entzündungs-versuche am Knorpel," Eberth's "Arbeiten," iii.), Wartmann ("Recherches sur l'enchondrome," Geneva, 1880), Kassowitz ("Die normale Ossification," Vienna, 1881). Further details will be given in the section on the Special Pathological Anatomy of the Bones.]

88. The **bones** have a very marked power of regeneration and of hyperplastic proliferation. The seat of this power is not so much in the osseous tissue itself as in those tissues which normally possess the power of bone-production ; these are the periosteum in particular, and in a less degree the marrow. In very many cases the periosteum alone performs the office of replacing a loss of bony substance. Many osseous hyperplasias are essentially the work of the periosteum. Cartilage has also some power of reproducing bone.

Fibrous tissues unconnected with the skeleton very rarely give rise to bony tissue. Such abnormal bone-formation is, however, not unknown in certain cartilaginous and fibrous structures, such as the dura mater, the laryngeal cartilages, the intermuscular septa, and inflammatory fibrous tissues.

The formation of new bone may occur in various ways, but it follows in general the lines of the normal process of ossification. The simplest mode is perhaps that in which the periosteum (or medullary tissue) gives rise to **osteoblasts** (*i.e.*, large multinuclear formative cells resembling fibroblasts). These come into contact and cohere, and then imbibing calcareous salts are transformed partly into homogeneous matrix-tissue, partly into bone-corpuscles. In other cases the formation of bone is preceded or accompanied by the formation of granulation-tissue. Owing to this the exact mode in which the bone-substance is generated may be somewhat masked ; but close investigation shows that here also osteoblasts are produced in the first instance, and that these are afterward transformed into bone. The proliferating periosteum very often produces cartilage to begin with. Part of this cartilage may then pass directly into bone by a peculiar transformation. Or the cartilage may be replaced by a medullary tissue abounding in cells ; and from this, by the agency of osteoblasts, the bone-substance may ultimately be produced.

Normal cartilage behaves in the same way as that produced by proliferation of the periosteum. Like the latter it may be transformed into medullary tissue and bone-trabeculæ. We have thus, in addition to the osteoblastic mode of bone-formation, a second or metaplastic mode, by which an already existing tissue is transformed into bone. As we have said, this occurs most frequently in cartilage ; but other fibrous and

sarcomatous tissues, by taking up calcareous salts, may in like manner be changed into bone. Their basis-substance is transformed into bony matrix-tissue, and their cells into bone-corpuscles (Arts. 90–92).

[Further discussion of the subject of pathological bone-formation will be found in the Special Pathological Anatomy. The recent memoirs of the following authors will serve to illustrate the main questions: Kölliker ("Die normale Resorption des Knochengewebes," Leipzig, 1873), Steudener ("Beiträge zur Lehre von der Knochenentwickelung," Halle, 1875), Strelzoff ("Die Histogenese der Knochen," Zürich, 1873), Maas ("Ueber Wachsthum und Regeneration der Röhrenknochen:" "Langenbeck's Arch.," xx.), Ziegler ("Virch. Arch.," vol. lxxiii.), Wolff ("Unters. üb. d. Entwick. d. Knoch.," Leipzig, 1875), Busch ("Deut. Zeitschr. f. Chir.," vol. viii.), Kassowitz ("Die Ossification," Vienna, 1881), Macewen ("Proc. Roy. Soc.," vol. xxxii.).]

89. In **muscular fibre**, striated and non-striated, regeneration and hyperplasia start primarily from the existing muscle-cells. Non-striated muscular fibres may possibly be developed from connective-tissue cells also. New muscular cells are produced by ordinary nucleus- and cell-division. In striated muscle, the so-called muscle-corpuscles grow into large cells, losing, meanwhile, their contractile substance, and multiplying their nuclei. They become elongated and spindle-shaped, and then become converted into striated fibres. It is highly probable that no other cells have the power of generating striated muscle-cells, but on this point opinions differ. Wounds in muscle are filled up by cicatricial tissue, when the superficial muscle-corpuscles have been destroyed.

Nerves and **nerve-cells** have but slight power of reproduction. It is very questionable whether ganglion-cells can be regenerated at all in adult individuals. We have no knowledge of ganglionic hyperplasia.

In the case of nerves themselves, both regeneration and abnormal multiplication occur, though only to a slight extent. In nerve-regeneration the axis-cylinder and sheath of Schwann are the first to be formed, and then the medullary sheath. New nerves are developed only from existing nerves; at any rate very serious doubts attach to the statements which have been made in the opposite sense. Opinions differ as to the part played by the cells of the neurilemma and by the existing axis-cylinder.

[The statement that non-striated muscular fibres may be developed from connective-tissue cells has been made by more than one observer (J. Arnold, "Virch. Arch.," vol. xxxix.; E. Neumann, "Arch. d. Heilkunde," x.). It appears certain that cells having at least the structure and appearance of non-striated muscle-cells are so developed; but no proof has been given that they have corresponding physiological properties.

With regard to striated muscle and its regeneration, Kraske, the latest writer on the subject, asserts positively that new muscle is produced only from existing muscle-elements. Ziegler's observations are in accordance with this. An embryological argument may be brought against the possibility of deriving voluntary muscle from connective-tissue. According to the Hertwigs ("Die Coelomtheorie," Jena, 1881) the striated muscle-fibres of vertebrates are of epithelial origin ; they arise from the epithelia of the body-cavities. They are thus in their genesis and descent distinct from the connective tissues. (Cf. Balfour, "Comp. Embryology," vol. ii., ch. 22.) On the striated muscle-cells of tumors see Art. 153. On the repair of nerves see Paget, "Surg. Path." Lect. 11; and Ranvier, "Hist. d. Syst. nerv.," 1878.

CHAPTER XX.

METAPLASIA.

90. A tissue is said to undergo **metaplasia** when it is transformed into another of a diverse kind; and that without passing through an indifferent blastema stage, with the characters of embryonic or formative tissue.

In the foregoing chapter we have more than once pointed out that, of the several tissues belonging to the connective group, one may pass into another by simple modifications, partly affecting the cellular elements, partly the ground-substance. Such modifications are of the nature of metaplasias. They are confined to the connective tissues—fibrous tissue, cartilage, bone, mucous tissue, and adipose tissue, are so to speak potentially convertible. No such relation holds between fibrous tissue and epithelium or muscle.

The processes involved in metaplasia have their physiological and embryological prototypes. Hyaline cartilage, for example, is specially prone to transformation; its matrix-substance often undergoes a mucoid softening on the one hand, or a change to fibrous tissue on the other. Hyaline cartilage is, in fact, at best a transitory structure in man; it disappears in ossification, partly by retrogressive changes, partly by transformation into other tissues such as medullary tissue and true bone. Simple areolar and adipose tissue are likewise prone to change; the *panniculus adiposus* or subcutaneous fat of the adult is in the fœtus a mucoid tissue.

Pathological metaplasias are, however, still more common than such physiological metamorphoses.

[The term metaplasia is due to Virchow, who has also fully investigated the significance of the processes included under it ("Virch. Arch.," vols. viii., lxxix., "Gesammelte Abhandlungen," 1856, pp. 500, 509; "Cellular Pathology," and fourth German edition, p. 70). The subject seems to have awakened but little attention; it well deserves it, however, for metaplasia plays no small part in pathological change.]

91. One of the commonest metaplasias of a connective tissue is that by which cartilage is transformed into mucoid tissue or into areolar tissue.

The first step in the process is the liquefaction or dissolution of the matrix into a mucous or limpid mass (Fig. 21). The capsules also dissolve away and the cartilage-cells are set free (*c*). These change their form (*b*), becoming spindle-shaped or branching; and they then cohere into a cellular reticulum such as is met with in mucous tissue. The matrix-substance does not always become true mucus; it may pass into a liquid of different composition. Such changes are met with in the cartilages of diseased joints. The areolar tissue may subsequently become filled with marrow-cells or with simple fat; in the last case the tissue is transformed into mere adipose tissue (*e.g.*, in rheumatic polyarthritis).

Cartilage also changes very readily into osseous tissue. Part of it becomes transformed into bony trabeculæ, part into medullary tissue. The latter is effected through the intermediate stage of areolar tissue;

FIG. 21.—Metaplasia of Cartilage into Areolar Tissue. × 400. (From a case of fungous arthritis; hæmatoxylin staining.) *a*, hyaline cartilage; *b*, tissue made up of branching cells; *c*, cartilage-cells, set free by dissolution of the matrix, becoming converted into connective-tissue corpuscles.

the former by the deposition of calcareous salts in the matrix, itself simultaneously undergoing change into gelatin; while the cartilage-cells pass into osteoblasts and bone-corpuscles. It often happens that the cartilage-cells proliferate abundantly during this process; it is not then strictly speaking a pure metaplasia.

Fibrous tissue, like cartilage, may also be transformed into mucoid tissue and bone. The changes in this case are similar to those described in the other. The fibres and fibrillæ disappear as the tissue becomes mucoid tissue; when it becomes bone, calcareous salts are deposited in the ground-substance. Here too cell-multiplication is not uncommon.

Conversely, osseous tissue may pass into fibrous tissue or cartilage, especially the former, as happens very frequently in senile bone-affections. The ground-substance of the bone becomes decalcified and fibrillated, while the bone-corpuscles become connective-tissue cells.

The fibrous structures found in tumors are, like the normal ones, liable to metamorphosis into others of the same class. The metaplastic processes resemble those in normal tissues. The highly cellular sarcomatous tissue is very prone to transformations; and these are generally such as to show that it is allied to the connective-tissue group.

92. Metaplasia is to be distinguished from the simple degenerations as well as from the proliferative processes. In degeneration no new tissue is formed, and what exists perishes. In proliferation new tissue is formed from a cellular matrix or blastema, which is the result of cell-multiplication. Metaplasia stands in a measure between these. New tissue is formed; but there is no cell-multiplication, or if there is it is quite subordinate.

From many points of view metaplasia seems related to the retrogressive processes. The transformation of a tissue into mucoid tissue is near akin to mucoid degeneration. The new or transformed tissue is moreover not infrequently an unstable and perishable one. On the other hand, proliferation is no uncommon accompaniment of metaplasia, which is thus brought into relation with the progressive or formative disturbances of nutrition. The factor of greatest importance, as regards the further development of the transformed tissue, is the behavior of the blood-vessels. If good vascularization is effected, the tissue continues to live and grow; if not, then retrogressive changes are apt to set in.

SECTION V.

INFLAMMATION AND INFLAMMATORY GROWTHS.

CHAPTER XXI.

THE EARLY STAGES OF INFLAMMATION—EXUDATION.

93. **Inflammation** is a term implying a whole series of processes partly vascular and partly textural; and these processes admit of a great variety of combinations. Inflammation being thus a complex of many elements, we are unable to give a definition of it that shall be brief and at the same time exact. We might say, indeed, that one or other element (such as that relating to the vessels) is characteristic of inflammation; but the whole content of the term cannot be fully indicated without describing the processes to which the term is applied.

From the time of Celsus, *i.e.*, from the first century A.D., four cardinal symptoms of inflammation have been recognized: namely *rubor, tumor, dolor, calor*—or redness, swelling, pain, and heat. To these we may generally add a fifth, the *functio læsa*, *i.e.*, impairment or arrest of the function of the inflamed part.

These cardinal symptoms are, as a fact, very easily and very frequently to be made out; especially in cases where the inflammation is sudden and intense. In other cases, and especially in chronic inflammations, one or other of the symptoms is generally absent, or beyond the reach of observation. The constitution of the inflamed tissue may also modify the symptoms; its texture and composition may be such that the redness, for instance, or the pain, or the swelling, may be absent.

94. Galen rightly attributed the redness to an increased afflux of blood, and the swelling to an increased exudation from the vessels. The vascular changes, which thus take the form of hyperæmia, have been the subject of special attention during the last twenty or thirty years. Many investigators indeed have regarded the vascular changes as constituting the essential feature of the inflammatory process.

Andral defined inflammation simply as hyperæmia. Henle, Stilling, Vacca, Lubbock, and others referred the dilatation of the vessels, the accumulation of blood in them, and the resulting exudation, to paralysis of the vessel-walls from excitation of the sensory nerves (the neuroparalytic theory); Hoffmann, Eisenmann, Jos. Heine, Budge, Bruecke, Cullen, and others, to spasmodic contraction of the vessels (the neurospastic theory). In the latter case, the contraction of the arteries and the consequent slowing of the blood-current were supposed to lead

to an afflux of blood through the neighboring vessels, but in an inverse direction. The result of this vascular disturbance was engorgement and exudation.

In opposition to these neuropathic theories, some authors, like Haller, Vogel, Koch, Emmert, Simon, Paget, etc., explain the inflammatory disturbance of circulation and nutrition by supposing that the normal attraction of the tissues for the blood is somehow intensified. Virchow has formulated this "theory of attraction" with the greatest precision. In his view, the tissue-cells are excited by the "inflammatory stimulus" to increased activity ; they thereupon attract to themselves more nutriment, and so are impelled to grow and multiply. The hyperæmia and vascular dilatation are the result of this intenser attraction. The essential and efficient factor in inflammation is thus the application of a "stimulus" to the cells, which excites them to increased activity.

Numerous experimental researches during the last twenty years (amongst which those by Cohnheim are perhaps the most fundamentally important) have shown that neither the neuropathic nor the attraction theory can be maintained. Mere dilatation or mere contraction of the vessels does not bring about the disturbances of the circulation characteristic of inflammation. The changes observed in the tissue-cells at the beginning of inflammation do not bear the character of productive or formative disorders of nutrition. There is no evidence of any influence exerted by the tissues on the vessels and the blood, which is at all of the nature of attraction. The changes in the tissue-cells are partly concomitant with those in the circulation, partly antecedent to them, and partly subsequent. The vascular disturbance is not dependent on any peculiar influence exerted upon the vessels ; it is the result of injury or deterioration (Samuel) of the vessel-walls, with or without an actual lesion of the tissues. To simplify the explanation of the entire process of inflammation, it will therefore be well to consider separately the vascular changes, and the textural changes.

[For an account of the contributions which English pathologists (notably Hunter, Goodsir, Bowman, Lister, and Burdon Sanderson) have made to our present knowledge of Inflammation, the student should consult Paget ("Surgical Pathology," Lects. 13–18), Simon and Burdon Sanderson (Arts. on "Inflammation," Holmes's "Syst. of Surgery," vols. i. and v.), and Burdon Sanderson ("Lectures," *Lancet*, 1, 1876, and "Lumleian Lectures," *Lancet*, 1, 1882). References to the work of others will be found below.]

95. **The vascular changes.** Cohnheim's researches were the first to make us accurately acquainted with the vascular disturbances connected with inflammation. He showed that these disturbances may be directly studied under the microscope. The object is usually some transparent vascular membrane belonging to a living animal. The most con-

venient is the frog's mesentery, which from its fineness is well adapted for microscopic examination. The frog, paralyzed with curare, is laid on its back on a large object-stage. The abdominal cavity is opened by means of a cut along the left side, and a loop of intestine is carefully drawn out. This is then spread over a thin circular cover-glass (10–12 mm. in diameter) surrounded by a thin ring of cork stuck to the stage with Canada balsam. The intestine is readily fixed to the cork ring by means of fine pins. If it is not desired to make a protracted examination, it is enough to fasten a cork ring (4–6 mm. thick) to a large object-stage with sealing-wax, and to spread out the intestine over that. The preparation need not be covered with a cover-glass. If no strain is thrown on the mesentery, and it ,as well as the frog is kept properly moist, the vascular changes may be observed for hours together.

[Further details of the method are given by Cohnheim in his various memoirs on inflammation and embolism ("Virch. Arch.," vol. xl. ; "Neue Untersuch. üb. Entzünd.," Berlin, 1873 ; "Untersuch. üb. d. embol. Processe," Berlin, 1872). The foot-web and tongue of the frog are also very convenient objects. The latter is to be turned out, spread over a cork ring, and fastened down with fine pins. Inflammation is then produced by a drop of acid, or by clipping out a fragment with the scissors.

For the study of the inflammatory process on a large scale the rabbit's ear is well adapted. Inflammation may be set up by rubbing it with croton oil (Samuel, "Berl. klin. Woch.," 24, 1866, and "Der Entzündungsprocess," Leipzig, 1873). The mesentery or omentum of a warm-blooded animal may also be employed, if proper precautions are taken to maintain the body-heat, etc. See Stricker and Sanderson, "Handbook for Phys. Lab.," 1870 ; Thoma, "Virch. Arch.," vol. lxxiv.]

96. The exposure of the mesentery to atmospheric air quickly sets up inflammation. The earliest vascular change is a general **dilatation** of the vessels, first of the arteries, then of the capillaries and veins. The **flow** of the blood through the widened channels at first becomes **more rapid**; but sooner or later the speed diminishes, and at length the flow becomes **slower** than the normal. The individual blood-cells, which at first were indistinctly seen as they hurried past, become recognizable, especially in the veins and capillaries. In these latter the blood begins to accumulate more and more as the current slows. In the veins the peripheral layer of the current, usually containing plasma only, begins to be filled with white blood-cells. These have left the axial stream, and float slowly on with the slower peripheral current ; or, fastening themselves to the wall, they remain immovable or oscillate to and fro. This is described as the marginal or **peripheral disposition** of the white blood-cells (Fig. 22, *d*). At this stage the red cells take the place of the white in the capillaries.

Before long the peripheral disposition of the cells is associated with another appearance. Here and there white blood-cells throw out processes which pass into the vessel-wall (*e*). Soon the processes appear outside the vessel (*e*), and thereupon the whole protoplasmic mass of the cell passes through the wall. The white cells in this way escape, migrate, or extravasate from the vessel (vein or capillary) by **diapedesis.**

The first white blood-cells which migrate are quickly followed by

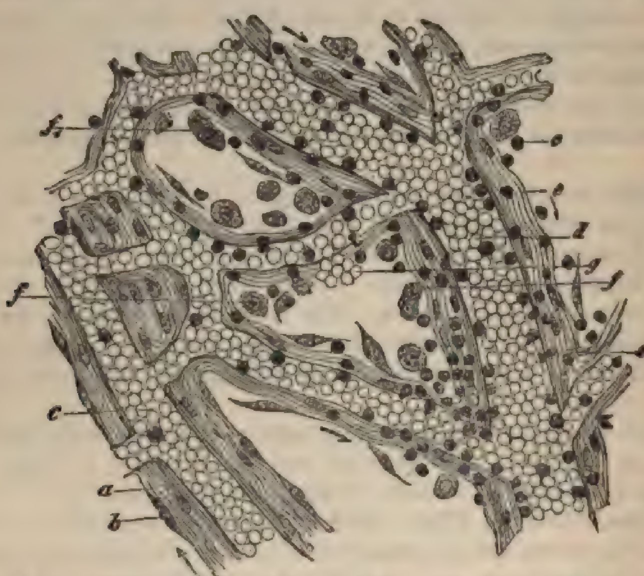

FIG. 22.—Inflamed Omentum from the Human Subject. *a*, normal fibrous trabecula; *b*, normal endothelium; *c*, small artery; *d*, vein with white blood-cells peripherally disposed; *e*, white blood-cells migrated or migrating; *f*, desquamated endothelium; f_1, multinuclear cell; *g*, migrated red blood-cells.

others, and in six to eight hours the veins and capillaries are surrounded by a multitude of white cells, or leucocytes, which gradually distribute themselves through the tissue by active locomotion.

From the capillaries, in which the circulation becomes very irregular and often stops altogether, there escape red blood-cells (*g*), as well as white. If the mesentery be slightly strained so that the circulation is brought to a stand-still (stasis) at some point, the migration ceases there. Blood-cells do not escape from the arteries.

Associated with the escape of the formed elements of the blood, there is always an **escape of liquid.** This is not in general directly perceptible, but is evidenced by the accumulation of liquid which takes place in the substance and on the surface of the mesentery.

This escaped liquid is comparatively rich in albumen, and thus differs essentially from the exudation which follows upon simple vascular engorgement. Moreover it coagulates readily, especially when it is effused on the surface of the mesentery.

[This description of the inflammatory process as observed in the mesentery applies also to that produced elsewhere, as in the frog's tongue, by caustics. In the latter case the process is not observed in the cauterized piece (which is in fact dead), but in its neighborhood. Thoma ("Virch Arch.," vol. lxxiv.) has shown that the process in warm-blooded animals is identical with that in cold-blooded animals.

W. Addison ("Trans. Prov. Med. Asso.," 1842–45) observed the escape of the white blood-cells from the vessels so early as 1842. Waller (*Phil. Mag.*, vol. xxix.) described the phenomenon more fully in 1846. The discovery was, however, completely forgotten until Cohnheim made it anew in 1867. Caton (*Journ. Anat. Phys.*, 1871) showed that the white cells escape even from healthy vessels, at least in the amphibia.

The peripheral disposition of the white blood-cells is a purely mechanical phenomenon (Weigert, Article "Entzündung," "Realencyclopädie der ges. Heilkunde"). It was first observed by Williams ("Gulstonian Lect.," 1841). Schklarewsky ("Pflüg. Arch.," vol. i.) has shown that a similar effect is produced when a slow stream of liquid, containing fine powders of various densities in suspension, is made to pass through a narrow tube. When the stream flows at a certain rate the lighter particles cling to the periphery, the heavier ones are hurried on by the axial current. This is what happens in the case of blood. When the current is slowed to a certain extent, the white cells go to the periphery ; when it becomes still slower (as in engorgement) the red cells go there also. (See also Appert, "Virch Arch.," vol. lxxi. ; Hamilton, "Proc. Roy. Soc. Edin.," vol. xi.).

The chemical composition of inflammatory exudations and inflammatory lymph has been investigated by Hoppe-Seyler ("Virch Arch.," vol. ix.), Reuss ("Deutsch. Arch. f. klin. Med.," xxiv.), F. A. Hoffmann ("Virch. Arch.," vol. lxxviii.), and Lassar ("Virch. Arch.," vol. lxix.).]

97. The effects of the process just described are easy to follow. The inflamed tissue becomes red, swollen, and hot ; we have the inflammatory flush, and the inflammatory exudation or infiltration. The pain felt is referable to pressure, tension, or chemical irritation, acting on the sensory nerves in the tissue. It is plain, too, that the function of the part must be injuriously affected ; the accumulation of exuded matter and the imperfect and disordered nutrition of the part are enough to account for that. The vascular disturbance is beyond doubt the most important and most characteristic factor in the entire process of inflammation. The other tissue-changes involved are not to be overlooked or undervalued ; but it is the disturbances in the circulation which give inflammation its special character, and determine its course. The question as to the essential nature of inflammation is thus almost reduced to the question of the causation of these vascular disturbances.

The slowing of the blood-current, the dilatation of the vessels, the peripheral disposition of the white blood-cells, the migration of these from

capillaries and veins, and the migration of the red cells from the capillaries, are all of them referable to a molecular **alteration in the vessel-walls** (Samuel). Mere paralytic dilatation does not give rise to slowing of the current, or to peripheral disposition of the white cells ; mere slowing of the current is not followed by extravasation of the cellular elements of the blood. Increased activity of the neighboring cells will not explain exudation, for white and red blood-cells will escape from the vessels into a tissue whose cells are already dead. Cohnheim has shown that if the circulation through a vessel is interrupted for a certain time (in frogs, from thirty-six to sixty hours), the vessel-wall undergoes such changes that, when the blood is again allowed to circulate, an exudation makes its appearance just as in inflammation.

The alterations in the vessel which take place in inflammation cannot be histologically demonstrated. We infer them from the fact that the vessel-wall becomes more permeable. We must suppose that the elements composing the vessel-wall are in some way loosened ; the cementing substance which unites the endothelial cells seems partially to give way. Arnold's researches make it likely that the cells transude chiefly at places where the intercellular cement is abundant. The slowing of the blood-current itself may probably be due to endothelial changes, in virtue of which the frictional adhesion between blood and vessel-wall is increased (Lister, Ryneck, Cohnheim).

[It may be accepted as an established fact that in inflammation the vessel-wall is affected (Samuel, "Virch Arch.," vol. xliii., and Cohnheim, *loc. cit.*). But it is still questioned by some whether the affection is of the nature of a chemical alteration, or a mere widening of pre-existing intercellular apertures. Arnold, who has worked much at the subject, formerly thought that small openings (*stigmata*) normally existed between the endothelial cells, and that these enlarged in inflammation into wider *stomata*. He based this theory mainly upon injection-experiments, which seemed to show that the vessel-wall was permeable, even to blood-cells. Cohnheim all along opposed the theory, and Arnold has now given it up. At the spots where *stigmata* were said to be we find nothing but little masses of cementing substance. Cohnheim argued against the existence of openings, from the fact that the exudation has not the same composition as liquor sanguinis. The fact that inflammatory exudation is richer in albumen and in cells, and so coagulates more readily than the liquor which transudes in simple engorgement, speaks for a change in the permeability of the vessel-wall. This has indeed been demonstrated by injection-experiments (Winiwarter, "Wien. acad. Sitzungsber.," lviii.; Arnold, *loc. cit.*). Cohnheim, like Hering ("Wien. acad. Sitzungsber.," lvii.), regards the escape of the elements of the blood as due to a process of filtration. He thinks the altered quantity and quality of the transudation (in inflammation as compared with health) are referable simply to an alteration of the vessel-wall, that is to say, to an alteration of the filter.

Thoma maintains ("Virch. Arch.," vol. lxxiv.), on the strength of certain experiments, that the white blood-cells never escape from the vessels unless they retain the power of independent movement. He would thus regard their migration as in some degree due to an active effort on their part. When the white blood-cells are deprived of the power of movement by irritating the mesentery with 1.5 per cent. salt-solution, the migration at once ceases.

On the causes of the slowing and stasis of the blood-current see Lister, "Phil. Trans.," 1858; Ryneck, "Rollet's Untersuch. Graz," 1870; Cohnheim, *Op. cit.*, 1873; Glax and Klemensiewicz, "Wien. acad. Sitzungsber.," lxxxiv.

The increased temperature of an inflamed surface is due merely to the increased circulation of blood through the part; the loss of heat not keeping pace with the gain. Cohnheim found by experiment that, in the same time, nearly twice as much blood flowed through the inflamed paw of a dog as through the non-inflamed one. This is quite enough to account for the rise of temperature.]

98. The causes of the alteration in the vessels are thus the causes of the inflammation. In other words, the alteration in the vessels is the direct or indirect consequence of the injury which excited the inflammation. Or still more accurately—any injurious agency which is capable of altering the blood-vessels in a particular way is capable of producing inflammation. It is clear then that the number of agencies capable of exciting inflammation is indefinitely great; they are beyond enumeration or separate discussion. All we can say is that mechanical, thermal, and chemical agencies (and especially the latter) may act so as to alter the vessels and produce inflammation.

The exciting cause of inflammation may operate in one of three ways. It is in the first place conceivable that the injurious agent (noxa) may primarily attack the vessels. This will be the case when it is brought to them in the blood itself. The surrounding tissue suffers only by a secondary effect. In the next place, there are cases in which the exciting injury affects both tissue and vessels at the same time. In a third instance, the tissue alone is injured; the alteration in the vessel-wall is secondary to alterations in the surrounding tissue. Of course these cases are not always completely independent. In the same case textural lesions and vascular lesions may intercombine in various ways at different times.

To produce inflammation an injury must be of a certain severity, and yet must not be too severe. Thus a slight wound of the corneal epithelium does not excite inflammation; the defect is simply filled up by regenerative proliferation. On the other hand, a powerful caustic applied to the skin produces at the cauterized spot not inflammation, but necrosis. Inflammation is indeed excited; but only in parts beyond the cauterized region. In these the caustic has not acted fully, so as to kill

the vessels ; it has merely altered or damaged them by chemical action. This example shows that there are no noxæ which can be described specifically as exciters of inflammation. Between the injury which is too slight to affect the vessels, and that which affects them too severely or kills them outright, there is an endless number of intermediate degrees.

The **repair of the damaged vessel-wall** is brought about by the *vis medicatrix* of the blood itself. If, when the injurious influence has ceased, the blood brings to the injured vessel the materials required for restoring it to its normal state, a *restitutio ad integrum* is effected. The inflammatory disturbance of the circulation thereupon comes to an end, and with it the exudation ; and the process of healing is begun.

99. **The textural changes.** Inflammatory change in the vessels must of necessity be associated with tissue-change, antecedent, concomitant, or subsequent. An injury from without which excites change in the vessel must always in the first instance affect a certain number of tissue-cells. By what is said in Arts. 78–80 we see that all such an injury can do is to set up disorganizing and degenerative changes in the cells. If the injury be slight, the cells may recover ; if it be graver, a certain number of them will perish. Multiplication is never induced by excitation of the cells from without.

When the injurious agent affects the vessels primarily, being brought to them by the blood, there are two events possible. If the noxa be very powerful, it will attack (or even kill) not only the vessel-wall, but the surrounding tissue also. If it is of trifling intensity, and its operation is thus confined to the vessel-wall, the surrounding tissue escapes in the first instance. It will be affected secondarily only when the injury to the vessel-wall is great enough to lead to inflammatory disturbance of the circulation, and so to disordered nutrition of the tissue.

Experiment and post-mortem observation have alike shown that in severe inflammation a certain number of cells invariably perish. The so-called "inflammatory stimulus" does not induce multiplication, but only degeneration and death, in the cells of the tissue. The slighter the inflammatory stimulus the less is the injury to the tissue. The degenerative and destructive effects of the exciting injury are least in the mildest forms of inflammation.

[Cohnheim's discovery of the migration of white blood-cells suggested a possible source of the extraneous cells found in all inflamed tissues, and in particular a possible source of pus. But the question has often been raised whether all these extraneous cells (round-cells or leucocytes) are derived from the blood. Before the discovery of migration, it was assumed that these leucocytes were the product of the multiplication of tissue-cells, excited to proliferate by the "inflammatory stimulus." But it was quickly seen that there were well-founded objections to this hypothesis. Cohnheim himself ("Virch. Arch.," vol. xl.) had shown, and that before he made his discovery, that it was impossible to suppose that

all pus-corpuscles arose from fixed cells; and that even the migratory connective tissue-cells of Von Recklinghausen were inadequate to produce the enormous multitude of cells found in pus. Numerous investigations made since then have shown that pus-corpuscles are derived solely from the blood, and that cells of the lymphoid type (such as pus-corpuscles) are never produced from fixed tissue-cells (Cohnheim, "Neue Unters. üb. d. Entzünd.," Berlin, 1873, "Virch. Arch.," vol. lxi.; Key and Wallis, "Virch. Arch.," vol. lv.; Eberth, "Unters. a. d. path. Inst. in Zürich," parts 2 and 3). As has been stated in the text, the tissue-cells either show signs of degeneration or perish outright, and in this condition mingle with the exudations.

This doctrine has not been without its opponents. Among the chief are Böttcher ("Virch. Arch.," vols. lviii., lxii.) and Stricker, with some of his pupils ("Studien aus d. Inst. für exper. Path. in Wien," 1870; various essays in the "Wien. med. Jahrb.," 1871–1880; "Vorles. üb. allg. Path.," Vienna, 1877–1879; "Internat. Encyclop. of Surgery," vol. i.). Böttcher's objections have been completely answered by the painstaking experiments of the observers above cited. Stricker's observations are admirably described by Burdon Sanderson in "Holmes's System of Surgery," vol. v. Recent researches have not tended to confirm the results on which Stricker's objections are based. Experimental researches on the origin of pus-corpuscles have generally been made on the cornea; as this has no blood-vessels it offers a favorable opportunity for discerning the parts played by the blood and by the tissue-cells respectively.]

100. The forms of necrosis and degeneration which may accompany inflammation are very various; they vary with the nature of the exciting cause, and with the intensity of the inflammation; with the character and extent of the vascular disturbance, and with the nature of the tissue. Any one of the forms of degeneration enumerated in Arts. 32–71 may occur. There is no rule determining in what cases any particular form shall appear. It deserves, however, to be specially mentioned, that a very common issue is the disintegration, solution, and liquefaction of the entire tissue—of its cells as well as its basis-substance. This is the case, for example, in all suppurations, to a greater or less extent. Another common occurrence is the coagulation of the exuded liquid, and also of the disorganized or necrosed tissue-cells. Fatty degeneration is not infrequently a secondary result of the vascular disturbance.

101. **Varieties of Inflammation.** Inflammation is a process which may affect any tissue possessing vessels, or in connection with vessels. In other words, it may affect any tissue in the body, except a few epidermoid structures. Its seat may vary greatly. It may lie within the parenchyma of an organ, or be confined to its surface; that is to say, we may have **parenchymatous** inflammation, or **superficial** inflammation. The former affects the interior parts of solid organs, like the glands, muscles, or brain. The latter form occurs on the exterior of the body, in mucous membranes, and in the lining membranes of the great serous cav-

ities. In the former the exuded liquid saturates the tissues, and is spoken of as an **infiltration.** In the latter it is deposited on the surface, and is spoken of as an **effusion,** or an **exudation** in a narrowed sense of the term. Parenchymatous inflammations are still further subdivided. Glands, muscles, and nerves possess a fibrous framework in addition to their specific elements. Inflammation of the former must be distinguished from that of the latter; we have thus **interstitial** inflammation, as distinguished from parenchymatous inflammation in a narrowed sense of the latter term. There is really no essential difference between the two. The only value of the distinction is—that it allows us to indicate briefly the seat of inflammation in certain organs, whose fibrous framework is well defined from the specific parenchyma. Thus interstitial inflammation of the liver implies that the chief inflammatory changes are to be found in the periportal fibrous tissue, the liver-cells being relatively less affected. If it is mainly the lobules which are affected, the inflammation is described as parenchymatous. Mistakes are often made by referring simple degenerative changes in the liver-cells to parenchymatous inflammation.

In speaking of the parenchymatous inflammation of a particular organ, it is customary to make use of a term compounded of the Latin or Greek name of the organ and the affix **-itis.** Thus hepatitis, nephritis, encephalitis, oöphoritis, refer respectively to the liver, kidney, brain, and ovary. In some cases old specific names are used instead, as pneumonia (for pulmonitis), an inflammation of the substance of the lung.

Histologists often indicate that an organ has undergone inflammation by saying merely that it is infiltrated with small cells or leucocytes. This accumulation of cells is in reality the feature by which the fact of antecedent inflammation is most readily recognized.

102. The histological characters of inflammation depend on the one hand upon the nature of the exudation, on the other hand upon the changes in the tissue. Both factors have been utilized in classifying the forms of inflammation, according as one or the other happens to be the more prominent.

With respect to **varieties** in the nature **of the exudation,** the following types are distinguished.

(1) **Serous** and **fibrino-serous** exudation. When the inflammatory alteration in the vessels is not very marked, the exuded fluid may be relatively poor in cells, and in its constitution may resemble the transudation from vessels that are merely engorged. It is, however, distinguishable from the latter by its greater percentage of albumen and of white blood-cells, and by its greater coagulability. Where it collects in quantity, therefore, it looks more or less turbid, and contains flakes and threads of coagulated fibrin. Collections of this fluid in serous cavities are described as fibrino-serous effusions. When it infiltrates the parenchyma of an inflamed solid organ, it gives rise to **inflammatory œdema.** When it is effused on the surface of the skin or of a mucous membrane, it is spoken of as **serous catarrh.**

(2) **Fibrinous** or **croupous** exudation. When the exudation contains fibrinogenic and fibrinoplastic elements in abundance, it undergoes coagulation throughout. As explained in Art. 35, the fibrinogenic substance is contained in the exuded liquid, the blood-cells yielding the fibrinoplastin. The presence of a certain percentage of leucocytes in the exudation favors coagulation. The term fibrinous exudation is especially applied to effusions into the various body-cavities. The coagulated masses form toughish, yellowish white, adherent films or coverings over the affected organs. When tissues are infiltrated, or mucous membranes covered over, with the coagulated exudation, the term croupous is generally applied to it.

The croupous **false-membranes** formed on mucous surfaces appear as yellowish white deposits, consisting chiefly of granular fibrinous trabe-

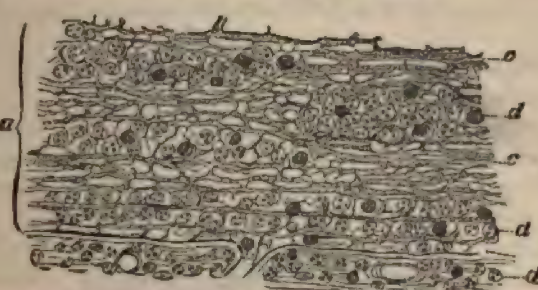

FIG. 23.—Section of a Croupous Membrane from the Trachea. + 250. *a*, false membrane; *b*, surface layer of the mucous membrane infiltrated with leucocytes (d_1); *c*, fibrin; *d*, pus-corpuscles.

culæ (Fig. 23, *c*) and filaments, interspersed with pus-corpuscles in varying amount.

In other cases, the false membrane is chiefly made up of hyaline flakes and lumps (Fig. 24, *b*).

(3) **Purulent** or **fibrino-purulent** exudation. When the migration of white blood-cells from the vessels is very extensive, and coagulation does not immediately ensue, the exudation assumes a whitish milky or creamy appearance. It consists simply of a liquid plasma and small leucocytes containing from one to three nuclei, and is called "**matter**" or **pus**. It is commonly the consequence of bacterial infection. The bacteria seem to act so as to hinder coagulation. When the purulent liquid contains in addition white flakes of fibrin infiltrated with pus-cells, the exudation is described as fibrino-purulent. It takes this form chiefly in inflammation of the serous membranes. When purulent infiltration leads to liquefaction and dissolution of the tissues, so that a pus-containing cavity is formed, we have what is called an **abscess**. If the loss of tissue is superficial, and a morbid surface is formed which secretes pus, we have an **ulcer**. Secretion of pus from the skin, mucous membrane, or synovial membrane, constitutes **purulent catarrh**. An infiltration, partly purulent and partly serous, is described as **purulent œdema**.

(4) **Hemorrhagic** exudation. Blood may be mingled with serous,

fibrinous, or purulent exudations, and is readily distinguished by its coloring them red. Such mixed exudations are called hemorrhagic.

(5) **Putrid** exudation. When from the presence of septic bacteria the exudation undergoes putrefaction, it is described as foul, putrid, or sanious.

103. We may likewise distinguish certain types of inflammation, according to the way in which the inflamed tissue is affected.

(1) **Desquamative catarrh.** In this form of inflammation, which affects the skin and mucous membranes, the epithelial cells are shed in large numbers and mingle with the secretion. It is also described as epithelial catarrh. Mucous catarrh is a variety of this distinguished by free mucus-secretion from the surface epithelium, or mucous glands.

(2) Necrotic inflammation. This term is applied to cases in which an

FIG. 24.—Section of Uvula from a Case of Diphtheria. × 100. (The epithelium has been shed; aniline-brown staining.) *a*, micrococci; *b*, sub-mucous tissue changed into amorphous flakes; *c*, infiltrated leucocytes; *d*, fibrinous exudation; *e*, blood-vessels; *f*, lymphatic vessel containing cells and fibrin.

inflamed tissue dies over an extent that is perceptible with the naked eye. The form of necrosis may vary; it may be simple necrosis, gangrene, mummification, caseation, or coagulation (Arts. 32–42).

A special interest attaches to inflammatory coagulative necrosis or **diphtheritic inflammation** (Art. 38). In this form, the tissue which has been killed by the injury causing inflammation, or by the inflammation itself, coagulates into large flakes and reticulated masses. This happens, for example, in diphtheritic inflammation of the uvula, where the epithelium and infiltrated subepithelial tissue are transformed into a coarse mesh-work interspersed with amorphous lumps and flakes (Fig. 24, *b*). The granulating tissue of a wound may, in like manner, become necrosed, and solidify into diphtheritic denucleated flaky masses.

Necrotic inflammation is of course always grave. It implies severe injury to the tissue, as well as serious alteration in the vessel-walls.

CHAPTER XXII.

LATER STAGES OF INFLAMMATION—RECOVERY—REGENERATION —GRANULATION—CICATRIZATION.

104. Inflammation ceases to advance so soon as the blood circulating through the vessels restores their walls to a healthy state. When this happens **recovery** at once begins.

After a slight inflammation, *i.e.*, one in which the vessel-walls are but slightly damaged, and the exudation trifling, the tissue affected may recover in a remarkably short time. So soon as the vessels perform their functions normally the exudation ceases to be formed; what is already effused forthwith undergoes **reabsorption** by the lymphatics or by the blood-vessels themselves. Simple serous exudations are those most readily absorbed, but corpuscular elements in moderate amount present no great difficulty. If any of the constituent cells of the tissue have been injured in the course of the affection, they may now recover. Their normal nutrition becomes possible as the circulation re-adjusts itself. In a short time nothing remains to show that inflammation has existed. The affected part becomes perfectly normal again.

If the inflammation has been more intense and the amount of exudation greater, and if in addition tissue-elements have been actually destroyed over a small extent, the process of recovery is somewhat different. When the circulation becomes normal the exudation is reabsorbed as before. Liquid and cells are alike taken up by the lymphatics and blood-vessels. Even coagulated exudations are gradually removed after undergoing liquefaction. The necrosed tissues, like the more solid masses of exudation, are ultimately disintegrated and liquefied, and then removed by absorption. If they lie on the surface they may be directly cast off (Arts. 112–115). If the loss of tissue be not too great, and the remaining parts are healthy and vigorous, **regeneration** or repair is effected by multiplication of the tissue-cells. Epithelium produces epithelium, muscle-cells form fresh contractile substance, periosteum generates new bone, etc. (Arts. 84–89). By and by the lost tissue is replaced by new tissue after its kind. It may sometimes even happen that the amount of new tissue produced is in excess of what is needed, and hyperplasia succeeds inflammation. This will happen when the excessive nutrition of the tissue, which usually follows upon inflammation, is kept up for a considerable time.

The magnitude of the defect which can be filled up in this way, and the fitness of the new tissue to replace the old, are matters depending on the regenerative power of the affected structures. As we know, this differs greatly in different tissues (Arts. 84–89). The lining epithelia are able to cover over large denudations of surface, and, as in catarrhal desquamation, may be reproduced again and again. But it would seem that brain-tissue has no power to form a single fresh ganglion-cell.

For the efficient causes which call forth regenerative or hyperplastic proliferation, we refer the reader to Arts. 78–82. Here we have only to remind him once more that it is not the agency or noxa which excited the inflammation which now excites the cells to multiply, by some kind of direct stimulus. Multiplication is completely independent of the original cause of the inflammation. It is simply the result of changes in the vital conditions or environment of the cells; and these changes are the result of the inflammatory process itself.

105. If the inflammation continues for a time and is not too intense, and if the circulation is not too seriously interfered with, so that a good blood-supply is continuously kept up, we have all that is needed for the production of **inflammatory tissue.** The cells which build up the new tissue are the migrated white blood-cells or leucocytes; the new tissue which they form is described as **granulation-tissue** and **cicatricial tissue.** The most important factor in this plastic process is the formation of new blood-vessels. These alone make it possible to keep the young formative tissue supplied with adequate nutriment.

The factors which cause the inflammatory process to take on a formative or constructive character are not always the same. We must in general assume that some cause is acting which keeps up the morbid alteration in the vessel-walls, and so gives the inflammation in some degree a chronic character. In open wounds the inflammation is kept up by contact with the air, with the floating matters suspended in it, with the dressings, with the secretions from the surface. This continues till the skin, growing over from the margins of the wound, at length protects the vascular tissue from further irritation. In subcutaneous necroses following on acute exudative inflammation, the dead tissues or dead exudations are enough to maintain a certain irritation in their neighborhood, especially as they undergo certain chemical changes before they are finally absorbed. In other cases, the original cause of injury persists and continues to excite ever fresh inflammation; or a new injury may affect a part in which inflammation is declining or overpast, and kindle it afresh. Which of all these possibilities applies to a given case is often hard to determine. Very frequently several such factors are in action, either at the same time, or at different stages of the process.

Plastic inflammation is, moreover, always associated with some form of degeneration. In parenchymatous organs, for instance, the growth of new fibrous tissue involves the atrophy or destruction of the proper

and specific elements. Intrinsic sources of irritation of this kind are thus seldom wanting, and they maintain the inflammatory process, even when the original exciting cause has ceased to act.

106. The new tissue produced as a result of inflammation often fulfils the purpose of replacing tissue that has been lost. This application of the process is apparent in the healing of wounds. In an open skin-wound, for instance, there is formed first of all a delicate grayish-red vascular formative layer, the so-called **granulating surface**. This in a way unites the borders of the wound. After a time it becomes covered over with skin, and is transformed into fibrous tissue. The breach is thus filled up, the separated parts united, and a scar is formed. The **scar** or **cicatrix** is thus the result of an inflammatory plastic process. Scar-tissue is formed in other organs in the same way, and with the same result of replacing a loss of substance.

In many cases, however, the production of new tissue by inflammation does not serve so useful a purpose. It often takes the form of a useless or injurious hyperplasia. This happens, for example, when after inflammation the corium of the skin thickens, or the papillæ become enlarged ; or when the fibrous tissue of the kidney or the liver is morbidly increased, giving rise to disturbances in the nutrition of the organ. Even the formation of adhesions and adhesive membranes connecting the organs of the great serous cavities is often accompanied by impairment and hindrance of their functions.

107. As we have just stated (Art. 105), inflammatory tissues are developed from extravasated leucocytes, in cases where the circulation has not been very seriously interfered with. This last ensures that the exuded corpuscles are speedily irrigated with a sufficient but not too abundant stream of plasma. These conditions are perfectly fulfilled in the aseptic healing of an ordinary wound.

If an open wound be observed twenty-four hours after it is inflicted, the bottom and edges will be found to be intensely red and somewhat swollen. The elements of the tissue are still quite distinguishable, though the tissue seems turgid, and here and there small necrosed shreds are visible. On the second day, the tissues have a more gelatinous appearance, the outlines of the tissue-elements (cells and fibres) are blurred, and the color is a grayish red. A reddish yellow liquid lies on the surface. After the second day little red nodules or granules begin to appear over the entire wound. These increase rapidly in size and number, and become at length confluent. After two or three days there is thus formed a continuous red granular layer—the granulating surface. It is covered with a more or less abundant secretion, which changes to a grayish gelatinous film, and afterward becomes more yellowish and creamy in consistence. This film is composed of an albuminous coagulable exudation and numerous leucocytes, some of them with one nucleus, but most of them with two or three small rounded ones. These are **pus-corpuscles**. They are not capable of further development, but are rather to be

looked upon as cells in process of decay. The multiplication of the nuclei is evidence, not of subdivision, but of disintegration.

The whole of the new tissue formed is derived from this delicate red formative or embryonic tissue, the granulation-tissue. From this the cicatricial tissue is developed.

[It seems beyond doubt that the multiple nuclei of pus-cells (Fig. 25, a_1) are simply the result of disintegration. Nothing has been observed to indicate that the division of the nucleus is followed by a division of the cell, and nothing is known of their further development. Besides, it is noted that the combined size of the multiple nuclei is not greater than that of the single nucleus. This shows that the partial nuclei have not the power, like true daughter-nuclei, of growing by assimilation of substance from the protoplasm of the cell (Küss, "De la vascularité et de l'inflammation," Paris, 1846; Paget, "Surg. Path.," Lect. 10).]

108. The naked-eye appearances in the healing wound are referable, partly to the accumulation of white blood-cells, partly to dilatation and distention of the vessels, and partly to the formation of new vessels. This latter takes place by means of off-shoots from the capillaries, as described in Art. 86. No other mode of vascularization has been certainly made out.

The development of granulations and cicatricial tissue takes place in the following way.

The injury sets up inflammation, which leads to an infiltration of cells at the borders of the wound. Large numbers of migrated cells (with a certain quantity of fluid) are thus accumulated. Meanwhile, parts of the existing tissue disintegrate by softening and liquefaction. A soft texture is in this way produced which is made up almost entirely of young round-cells, with very little intercellular substance. Some of these cells, chiefly those containing several fragmentary nuclei (Fig. 25, a_1), cease thereupon to live, and form true pus-corpuscles. They are either thrown off with the secretions from the wound, or are absorbed, or dissolved *in situ* and utilized to feed the more vigorous living cells. On the other hand, another set of (uninuclear) cells (a) begin to grow. Their protoplasm increases in amount and becomes more markedly granular (Fig. 25, b). At the same time the cloudy finely granular rounded nucleus becomes clearer, oval, and vesicular (b). The nuclear juice and nuclear substance become distinct, so that it becomes possible to discern clearly a nuclear membrane, nucleoli, and nuclear granules and filaments. This differentiation of the elements of the nucleus gives the cell an altogether different aspect and habit. It resembles an epithelial cell, or as it is phrased—it becomes **epithelioid**.

The transformation of leucocytes into epithelioid cells is accompanied by cohesion of the protoplasm of separate cells. A growing cell may

appropriate the substance of others which are decaying ; or two equal cells may coalesce to form a single one.

The epithelioid cells are the formative cells of the granulation-tissue ; they alone have the power of producing new connective tissue. They are best described as **fibroblasts.** They are usually uninuclear, and their numbers increase partly by successive transformations of round-cells, partly by subdivision. Very probably the division of their nuclei is of the karyokinetic type. If the protoplasm does not subdivide for

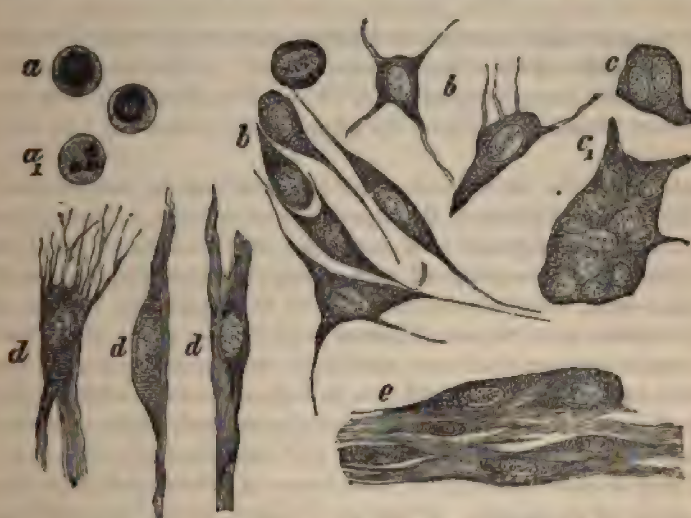

FIG. 25.—Granulation-cells in various stages. × 500 (Picrocarmine staining.) *a*, uninuclear; a_1, multinuclear migrated white blood-corpuscles : *b*, various forms of uninuclear formative cells ; *c*, binuclear ; c_1, multinuclear formative cell ; *d*, formative cells developing into connective tissue ; *e*, developed connective tissue.

some time after the nucleus has divided, binuclear (*c*) cells are formed ; and even in some instances large multinuclear cells, the so-called **giant-cells** (c_1). In healthy granulations giant-cells are produced but sparingly.

[Ziegler has endeavored to prove experimentally that the migrated white blood-cells are capable of further development, and are the primary source of cicatricial tissue ("Exper. Untersuch. üb. d. Herkunft d. Tuberkelelemente," Würzburg, 1875, and "Untersuch. üb. path. Bindegewebs- und Gefässneubildung," Würzburg, 1876). He made a small, disc-shaped chamber by fastening together two thin cover-glasses a slight distance apart. This was inserted under the skin of a dog and left for a certain length of time. When it was removed its contents could be examined microscopically. The thin interspace was found to be filled with cells, which either perished and broke up or underwent further development. In a single layer of cells obtained in this way, there were always some undergoing progressive change, and they could be observed with great ease. Thus not merely at the borders, but over the whole field, cells were

found in all stages of development from the lymphoid to the epithelioid and giant-cell type. The actual formation of tissue from them could be followed. When large cells are formed, a certain number of the round-cells in their neighborhood disappear. It is as if their protoplasm were appropriated by the larger growing cell. This is less surprising, as we know that migratory cells frequently pick up molecular matters (such as cinnabar) which they find in their way. The only difference is that the protoplasm is assimilated and utilized for growth ; the cinnabar of course is not.

The various stages of nucleus-division cannot as yet be described in detail ; only some of them have been observed. So far as is known, they correspond with the scheme of Arts. 74 and 75. Now and then a radial arrangement of the granules of the protoplasm is observed near the poles of the nucleus.

Ziegler's results have been called in question by various observers (Ewetzky, Weiss, Böttcher, Baumgarten, and others). These observers maintain that the migrated cells have no power of further development, and attribute the formation of new tissue to the multiplication of the fixed tissue-cells, especially in the case of the epithelia. Their experimental methods have been so different from Ziegler's, and their criticisms rest so much more on their own special theories of inflammation than on the facts adduced, that it is difficult to find a common basis for the discussion of them. Those who have used similar methods have in the main arrived at similar results. Senftleben ("Virch. Arch.," vols. lxxii. and lxxvii.) introduced fragments of dead lung, or artery-wall, into the peritoneal cavity of an animal. Tillmanns ("Virch. Arch.," vol. lxxviii.) used bits of hardened organs with artificial cavities in them. Hamilton ("Sponge-grafting," *Edin. Med. Journal*, 1881), introduced bits of sponge. All of these have found that the cells which migrate into the receptacles thus artificially provided undergo further development. Heidenhain had already discovered large cells in round bits of elder-pith, which he had inserted into the abdominal cavity of guinea-pigs ("Ueber d. Verfettung fremder Körper in der Bauchhöhle," Breslau, 1872). Schede ("Arch. f. klin. Chir.," xv.), Aufrecht ("Virch. Arch.," vol. xliv.), Bizzozero ("Annali universi di medicina," 1868), and others had already observed facts which were in favor of the notion that development does take place in migrated cells.]

109. The newly formed fibroblasts are rounded cells (Fig. 25, *b*). They soon change their form, however, by sending out processes and becoming elongated. In this way cells are produced which are club-shaped, spindle-shaped, or branched (*b*) ; and these cohere and coalesce in various ways. Meantime the larger formative cells are multiplied till at length they outnumber the small round-cells. Here and there they become tightly packed together. This is especially noticed in the deeper layers of the granulation-tissue. When their number has reached a certain

point, fibrous tissue begins to be produced by the formation of a fibrillated intercellular substance. This latter arises in part directly from the cell-protoplasm, and in part from a homogeneous ground-substance derived from the fibroblasts. In the first case, from the ends and lateral borders of the formative cells (*d*) there grow out fine fibrillæ, which unite with those of the neighboring cells. The direction and extent of the fibrous strands thus produced are independent of the original form and disposition of the formative cells. The run of the fibres is generally in the same direction for considerable lengths. When the fibrillæ have reached a certain degree of definiteness and strength the process of fibrillation ceases, and the remaining cells with their nuclei remain as fixed connective tissue-cells (*e*). They lie along the surface of the fibrous bundles. The process is thus completed—granulation-tissue has become **cicatricial tissue.**

The formation of **new vessels** starts as soon as the first formative cells are developed. It proceeds rapidly, and even in a day or two multitudes of vascular loops are already produced. They bring the granulations the nutriment they need, and supply cells to fill the vacancies occasioned by absorption of the first leucocytes. The only part taken by the epithelioid cells in vascularization is—that they serve to strengthen the thin-walled new capillaries, by disposing themselves along the outer surface of the vessels. It is possible that fibroblasts may now and then take part in the formation of new vessels. This they may do by attaching themselves to the budding off-shoots, and thus assuming the form of buds themselves. By excavation of their contents they are then converted into permeable channels.

Giant-cells, when they are present, seem to play no special part in the transformation of the granulations. They form fibrous tissue in the same manner as the other fibroblasts.

[Ziegler has observed the process of scar-formation from granulation-tissue, both in ordinary granulations and by the cover-glass method. The latter yields preparations which are better than any sections, inasmuch as all the cells and cell-structures remain *in situ;* there is no possibility of disintegration or disturbance of the natural relations. Tillmann's (*loc. cit.*) observations agree with Ziegler's.

The assertion is often made (Billroth's "Surgical Pathology," Rindfleisch's "Pathological Histology") that granulation-tissue passes into spindle-celled tissue. This is only partially the case. Spindle-cells are formed often enough, but the cells are just as often of many diverse shapes.

The granulations, when they are first formed, are nourished by the plasma which escapes from the existing vessels. Thiersch has shown that the spaces in which this circulates among the granulations may be injected from the blood-vessels. This mode of nutrition is, however, inadequate for the complete formation of the embryonic tissue ; new vessels are therefore required.

Ziegler (*loc. cit.*) and Brodowski ("Virch. Arch.," vol. lxiii.) have described a special relation of the giant-cells to the process of vascularization, but this is no longer maintained.]

110. The constructive processes taking place in the wound are completed when the cicatricial fibrous tissue is formed. The subsequent changes are limited to a certain amount of shrinking or contraction in the new tissue, and the suppression of some of the new blood-vessels. The scar, which from its vascularity is at first decidedly redder than its surroundings, begins to pale; and at length becomes paler and whiter than its surroundings. A depression frequently results from the shrinking of the cicatricial tissue. The smaller the wound the smaller and less marked is the scar.

This form of healing, in which the wound is closed by means of its own granulations, is called healing by **second intention.** Healing by **first intention** occurs when two wounded surfaces come into contact and grow together without the intervention of visible granulations. In principle the process is the same as in the first case. An inflammatory infiltration is produced, and in this new vessels and new fibrous tissue are developed. The difference is merely quantitative. In skin-wounds, for example, the exudation and granulations are so insignificant in amount that they are imperceptible; they are very quickly bridged and covered over by regenerative multiplication of the epidermal cells.

The chronic inflammatory processes leading to fibrous hyperplasia follow in general the same course as when new tissue is being formed. In different organs, however, there are special peculiarities to be noted. They will be treated of in considering the special pathology of the several organs.

111. While cicatricial tissue is forming in an organ by means of granulations, it usually happens that the **fixed tissue-cells** also begin to multiply by subdivision. The extent to which this multiplication goes on, and the share it contributes to the final result, are by no means constant. But they are by no means negligible, especially in long-continued inflammations. Hence the different importance assigned to such cell-multiplication by different observers. Some ascribed all formation of new tissue to it, denying the existence of the inflammatory process above described. Others allow it small significance, or ignore it altogether. The truth is probably this—that, accompanying the inflammatory constructive process, there is always some regenerative proliferation in the tissue, and that this is in inverse relation to the severity of the inflammation. Epithelium is a tissue which cannot be reproduced by means of granulations; it can be reproduced only by regenerative proliferation. Other specially differentiated tissues, such as muscles, nerves, bones, vessels, are in the same case. These, if replaced at all, must be replaced by regeneration starting in pre-existing homologous tissues. Cicatricial tissue pure and simple is therefore devoid of all such specialized structures, with the one exception of vessels.

If we were to define granulation-tissue according to its apparent purpose we might say that it is a structure fashioned out of the cellular material gathered by the blood from the system in general, and utilized to make good a defect which the fixed tissue-cells of the injured region are unable to repair. This final purpose, unfortunately for teleology, only appears in the process by which wounds are repaired. It is not apparent in the fibrous hyperplasias of glandular organs, or in the formation of adhesions and false membranes; but the mechanism is the same.

CHAPTER XXIII.

IMPERFECT RE-ABSORPTION—FOREIGN SUBSTANCES.

112. The **re-absorption** of inflammatory exudations is not always so complete as we have hitherto assumed (Art. 104). Though it is true that in most cases even exudations containing numerous corpuscular elements are sooner or later absorbed, still there are limitations to this; or it may be that circumstances arise which directly check or hinder the process. If re-absorption (or briefly resorption) does not ensue, further changes take place in the exudation, whether it be an effusion into a cavity or an infiltration of a tissue. The commonest result is condensa-

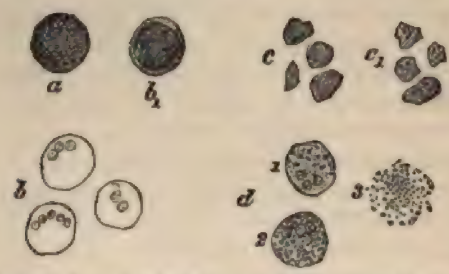

FIG. 26.—Pus-cells becoming fatty and shrinking. × 400. *a*, pus-cell in solution of common salt; *b*, pus-cell treated with acetic acid; b_1, so-called granulation-cell; *c*, shrunken pus-cells; c_1, shrunken and fatty pus-cell; *d*, pus-cells that have become fatty and broken up (Gluge's corpuscles).

tion, depending on loss of water and caseation. In purulent effusions, for example, the pus-cells undergo fatty changes (Fig. 26, *d*, "Gluge's corpuscles"). They then shrink and break up, so that presently all that is left is a mass of small irregular lumps (*c* and c_1), and granular detritus (d_3). The watery parts of the exudation being more or less absorbed, these products of disintegration form a creamy or cheesy pulp. Fibrinous effusions may also be transformed into a mass of cheesy detritus. These not infrequently become calcified as time goes on.

Condensed effusions of this kind may long resist resorption. It often happens that they cannot be removed in this way at all. Infiltrated tissues which have necrosed may, in like manner, resist resorption, and so persist for an indefinite time. Dead bone and fascia especially, which are hard to liquefy or disintegrate, may long be retained. But softer tissues

may likewise become incapable of resorption, when necrosis has resulted in their caseation or mummification.

113. Tissues which have been killed by the original injury or by the subsequent inflammation, and inflammatory exudations, are no longer parts of the organism. They are **foreign substances,** and they act as such. In other words, they set up and maintain inflammation in their neighborhood. They act like foreign bodies thrust forcibly into the tissues from without. Necroses other than inflammatory, such as those resulting from ischæmia, and hemorrhagic effusions or extravasated blood which has become necrosed, all act in the same way as foreign substances. To the tissue affected by them it matters nothing whether they once belonged to the organism or not. It is of more importance to consider the physico-chemical nature of the foreign substance. This it is which determines the intensity, the extent, the general character of the inflammation induced.

The great importance of the inflammations excited by such dead or foreign substances makes it absolutely essential to have a clear conception of their nature. And we must in especial discover the characteristics of the inflammation set up when the foreign substances are of corpuscular size. Stated generally, we may put it—that in such a case we have in addition to the ordinary phenomena of inflammation other processes whose object is the removal of the foreign substance. The peculiarities of special cases depend on the physico-chemical nature of the substance.

Foreign substances may be divided into two groups:—those which have but a slight effect or none in altering the surrounding tissue, and those which act destructively and excite violent inflammation. Among the first group are some substances easily absorbed, and others which are absorbed with difficulty.

114. The easily absorbed substances include liquids and small solid matters which have no intense chemical action on the surrounding tissue. Of this latter kind are, for example, cinnabar, which is rubbed into the skin in tattooing; the dust of coal, lime, or iron, which is inhaled and passes from the alveoli into the lung-tissue; and lastly, fatty and disintegrated exudations, softened and disintegrated tissues, and such like.

The effects produced in the organism by small corpuscular bodies of the above kinds are not serious. Perceptible inflammatory changes are brought about only when large quantities of them are present together; their effects are thus integrated as it were.

Most of the pulverulent or corpuscular matters referred to are removed from the tissue containing them by resorption. If they lie within a liquid exudation (as do fatty pus-cells or free oil-globules) they may be taken up along with it into the lymphatics, and so carried off. A large number of them would still, however, remain, if another means were not at hand for disposing of them. The additional resource is brought into play by the mild inflammation which the foreign substance excites. The agents

are the white blood-cells which thereupon migrate from the blood-vessels. These migratory cells appropriate the foreign substances lying in the tissue (Fig. 27, h, h_1, h_2, h_3). They let their protoplasm flow round them, and so take them up into their interior. By frequent repetition of this process granule-carrying cells are produced. According to their contents, these have been variously described as fat-granule carriers (h_2), blood-cell carriers (h_3), pigment-granule cells (Fig. 28, c), dust-cells, cinnabar-carrying spherules, etc. In cerebral degenerations, we constantly find cells containing granules and minute drops (Fig. 27, h_1, h_2); these

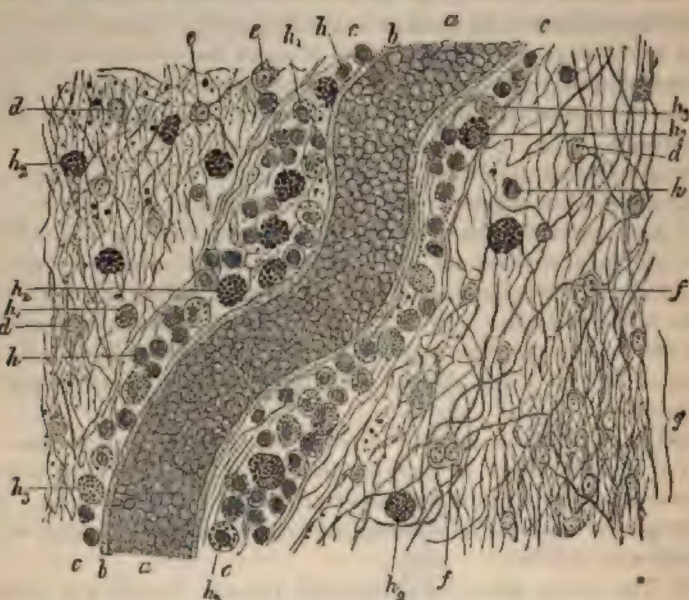

FIG. 27.—Section through a Degenerating Patch from the Brain. × 200. (Osmium preparation.) *a*, blood-vessel filled with blood; *b*, tunica media; *c*, adventitia with its lymph-sheath; *d*, unaltered neuroglia-cells; *e*, fatty neuroglia-cells; *f*, binuclear neuroglia-cells; *g*, sclerosed tissue; *h*, round cells; h_1, round-cells containing single oil-globules; h_2, fat-granule carriers; h_3, pigment-granule cells, some containing blood-cells.

are migratory cells, which have taken up some of the products of disintegration of the brain-substance.

The carrier-cells ultimately reach the lymphatics. Thus in the brain they accumulate in the lymph-spaces surrounding the adventitia of the arteries (Fig. 27, c). Hence they are carried on by the lymph-current, and at length reach the lymphatic glands. Here they are retained for a time, and ultimately filtered away—at least in part. In Fig. 28 is represented a lymphatic gland infiltrated with pigment-carrying cells; these were derived from an extensive hemorrhage which had undergone resorption. The pigment-carriers for the most part remain within the lymph-sinuses; only a few have penetrated the follicles. The greater portion of the foreign substance absorbed usually remains in the lymphatic gland; but it

may happen that a part filters through it and reaches the next gland, or ultimately the blood-vessels. A considerable quantity of corpuscular foreign matter can in this way be removed. Often, however, the absorption is inadequate, and a portion of the substance remains *in loco*.

Foreign substances may be deposited along the walls of the lymphatics as well as in the glands. The granules inclosed in the carrier-cells are set free as the cells decay. Hence it often happens that lymphatics, which have conveyed away quantities of pigmented substance, show traces of pigmentation all along their course. This happens likewise in the corresponding glands. The deposits may even excite the respective tissues to inflammatory hyperplasia.

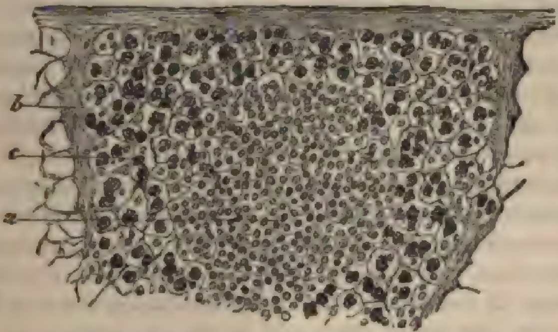

FIG. 28.—Section of a Lymphatic Gland whose Sinuses and Alveoli contain Pigment-granule Cells. × 60. (Carmine staining.) *a*, follicle; *b*, trabeculæ; *c*, pigment-granule cells.

The above process is, of course, only carried out in its entirety when the foreign substances are insoluble and indestructible. Soluble and destructible matters like chalk, fat, myeline, are sooner or later dissolved or attacked; the agency of the cells, of oxygen, or of non-organized ferments completes their destruction.

[References:—Virchow's "Cellular Pathology;" Ponfick, "Virch. Arch.," vol. xlviii.; Rindfleisch, "Exper. üb. d. Histol. des Blutes," 1863; Orth, "Virch. Arch.," vol. lvi.; Bizzozero, "Med. Jahrb.," 1872.]

115. The process of resorption and the associated inflammation are somewhat different in character when the foreign substance forms a compact mass, offering more or less resistance to removal. Such are, for example, ligatures, drainage-tubes, ivory pegs, leaden pellets, necrosed bone, compact hemorrhagic patches, hæmatomata and infarcts, thrombi, coagulated or condensed exudations, necrotic cheesy masses, etc.

All of these excite in the surrounding tissue a certain amount of inflammation, though its intensity is very various. If the foreign body is quite insoluble in the juices, as glass is, and if the introduction of it is unaccompanied by any injury to the tissues among which it lies (*e.g.*, in

the abdominal cavity,) then the effect may be almost nothing. Bodies which are soluble, and undergo chemical changes in the tissues, usually irritate them much more, and the inflammatory processes excited are generally intense. This is also true of bodies (like bullets) which produce laceration as they penetrate the tissue.

The first stage is the formation of a zone of inflammatory infiltration around the foreign body. This is followed by the development of granulation-tissue, and at length of fibrous tissue. If the foreign body is not meanwhile absorbed, it thus becomes encapsuled. Only insoluble and compact bodies can remain quite unaltered, for resorption is as it were attempted, even though it be in vain. Bodies which are at all assailable are sure sooner or later to undergo changes. These ensue as follows: the migratory leucocytes, transformed into uninuclear or multinuclear formative cells, attach themselves to the surface of the object. If this be made up of smaller parts, or if particles of necrosed tissue be mingled with it (such as decomposed blood in hemorrhagic patches), these are taken up by the cells and carried off in the manner set forth in Art. 114. If the body be compact and not to be broken up, the cells cling to its surface. If there be accessible cavities or clefts in it, they penetrate into these. If the cells be insufficiently nourished, they become fatty and die. If new vessels are formed to supply them, they develop as granulations. Very often indeed multinuclear or giant-cells are found in such circumstances. A dead piece of bone inserted under the skin of an animal, and examined a few weeks after, will be found interpenetrated with vascular granulations, and the trabeculæ will be beset in many places with giant-cells. The whole process is very similar to that of physiological bone-resorption. By means of the clinging cells blood-clots, necrotic patches, inserted pieces of dead liver or lung, ligatures, etc., are absorbed amid the granulations. They are partly softened and dissolved, partly broken up and carried away.

This process is peculiarly modified when the foreign substance is firmly connected with the surrounding tissue; when it is in fact a necrosed fragment of the tissue itself, such as bone or kidney. In this case the first step is the separation of the living tissue from the dead. At the common boundary of the two an inflammatory zone is formed, which by the softening and resorption of the border-tissue leads to the loosening of dead from living. This zone is called the **zone of demarcation**; the loosened piece is a **sequestrum**. The sequestrum is by and by broken up and absorbed. If it lies on the surface it is thrown off as a **slough**; it leaves an **ulcer** behind it.

A further modification ensues when the foreign substance simply lies on the surface of an organ. This occurs, for example, in the fibrinous effusions which form on the surface of the pleura. The deposit is in this case invaded by granulations and cicatricial tissue from one side only. If it lies between two separate organs or lobes it may be invaded from both sides.

[Langhans (" Virch. Arch.," vol. xlix.) was the first to describe minutely the processes by which the larger foreign bodies are absorbed. He pursued the subject experimentally by producing extravasations of blood in various animals. He thus discovered the giant-cells. Heidenhain (" In. Diss.," Breslau, 1872) also found them in pieces of elder-pith, which he had inserted in the abdominal cavity of animals. Ziegler always met with them on the surface of his cover-glasses (Art. 108). By introducing bits of boiled bone into the abdomen of animals, he found that granulations always penetrated to the interior, and that large **osteoclasts** or resorption-cells (with one or many nuclei) were developed in contact with the bone. Senftleben (" Virch. Arch.," vol. lxxvii.) and Tillmanns (" Virch. Arch.," vol. lxxviii.) have gone further into the matter, and find that hardened aseptic animal tissues, such as bits of liver, kidney, or lung, are partly absorbed and partly adhere and heal in. Fresh tissues are absorbed faster than hardened tissues. Hegar (" Klin. Vorträge," No. 109) and Rosenberger (" Langenbeck's Arch.," xxv.) have shown that absorption is most speedy in the case of tissues taken quite fresh from a living organ, and introduced into the body. The inflammatory reaction is very slight and ends with the process of resorption. The resorption of bone has excited special attention. Kölliker (" Die normale Resorption des Knochengewebes," Leipzig, 1873) and Wegner (" Virch. Arch.," vol. lvi.) have studied it minutely. They as well as others have made out this process to be something quite peculiar. Ziegler (" Virch. Arch.," vol. lxxiii.) has sought to do away with the attempted isolation of the process, and to put bone-resorption on a level with other resorptions. He thinks it possible to view all processes of resorption from the same stand-point. In every case the process is carried out with the purpose of removing from the organism a substance which is foreign and useless to it. Giant-cells are very usually formed in such circumstances, and it is possible that they take up the soluble parts of a tissue when it undergoes liquefaction. But resorption is not confined to their agency ; it goes on where they are absent. It remains a remarkable fact that they should so frequently be found on the surface of solid objects. It is perhaps conceivable that the contact of the cell with a foreign body hinders in some way the process of cell-division, without affecting the subdivision of the nucleus.

It has long been known that foreign bodies may " heal into " a tissue. Details of the histological process will be found in the memoirs quoted above. Hallwachs has lately published some observations on the subject (" Langenbeck's Arch.," xxiv.).]

116. Many foreign substances, and especially certain altered organic products, have a far more baneful effect on the surrounding tissues than any we have yet considered. Such, in a high degree, is dead tissue which from contamination with septic matters has passed into a state of putrid decomposition.

In the course of this decomposition various chemical compounds are formed which act harmfully on the tissue (Art. 42), and set up in it progressive destructive changes, and violent hemorrhagic or purulent inflammation. Under the action of the pus-cells, which form in great quantity, and of the septic ferments, the necrosed tissue becomes dissolved. If it is connected with living tissue, a suppurative zone of demarcation is formed and sets it free; the result is a cavity filled with pus—an **abscess**. The process often continues, the infiltration and dissolution of tissue go on, and the abscess grows larger and larger.

If decomposing matter from the abscess reach the blood-vessels or lymphatics, and is so conveyed to other regions, it may lead to putrid decomposition and purulent inflammation at the spots where it lodges. In this way **metastatic abscesses** are formed.

If the inflamed region be near a free surface and at length breaks through it, we have a **suppurating ulcer** formed.

Should death not result from this destructive suppuration or purulent necrosis, the injury done may be repaired by the formation of granulation-tissue at the boundary of the living tissue and the dead. In the course of time the pus secreted may be absorbed, or solidified and encapsuled.

CHAPTER XXIV.

THE INFECTIVE GRANULOMATA.

General Characters.

117. The granulative formations we are about to discuss are all distinguished by similar characters. Their development usually stops short at the fibroblast stage, and having reached it (or even before that) the constructive process gives place to retrogressive changes. Cicatricial development being arrested, the granulation-tissue persists for a time unmodified, and often develops to a considerable amount. For this reason Virchow described the formations as **granulative growths** or **granulomata**. All these growths have furthermore the clinical character of **infectiveness**. Hence they have been termed infective growths by Klebs and Cohnheim, and specific inflammations by Rindfleisch.

Their infective character may be recognized by various signs. Thus they are all locally **invasive**, *i.e.*, the granulation-tissue spreads centrifugally from a centre into the surrounding structures. At the same time the central (or oldest) part of the new formation usually dies and disintegrates. In many cases the lymphatic system becomes affected, so that secondary granulative foci are formed in it. From the lymphatics the process is at times transferred to the blood; or it may invade the blood-vessels directly. The final result is the spread of the disorder to various organs, or throughout the system.

In most of the granulomatous disorders we may have not merely a diffusion of the disease throughout the individual organism, but also a transference of it from one individual to another; the affection is **inoculable**. If one person be inoculated with the inflammatory products derived from another, he acquires a disease whose course is exactly similar to that of the original one, and which yields identical inflammatory products. This latter character of infectiveness is that by which it is most readily recognized.

To this group of infective granulomata belong the neoplastic formations found in tuberculosis, syphilis, leprosy, lupus, glanders, and actinomycosis. All these affections are due to the invasion of the body by a virus or poison derived from the outer world, or from the body of another individual. This virus may probably be produced by vegetable parasites. In leprosy (Armauer Hansen, Neisser), tuberculosis (Koch),

and syphilis (Klebs) bacteria have been found, and in actinomycosis a special fungus. These are declared to be the originating causes of the respective diseases. Our ideas as to the nature and character of these affections are as yet mainly based upon their clinical course; but we have also derived something from inoculation-experiments. Tuberculosis and syphilis are thus known to be communicable from one person to another; tuberculosis is also communicable from man to lower animals.

[It was Virchow who invented the term "granulative growth" or "granuloma" for these formations, which he was the first to define accurately ("Die krankhaften Geschwülste," ii.). He set it down as characteristic of them—that they usually fail to develop beyond the stage of granulation-tissue; that this is unstable in character; and that the regular issue is in ulceration. He laid stress on their near alliance to the products of inflammatory processes. Klebs ("Prager Vierteljahrsschr." vol. cxxvi.) called such growths "infective growths or tumors," and the name has been adopted by Cohnheim. Neither description is exactly adequate. Virchow's takes no account of their infective character; Klebs's bears no reference to their structure. As it is by no means certain that there are no other new formations of infective origin, some apter designation seems called for. Even Rindfleisch's term "specific inflammation" is too indefinite, for it might perfectly well apply to a number of other processes, such as those of pyæmia, erysipelas, variola, etc. In this book the term "infective granuloma" will be used; this serves to keep in view both the structure and the clinical character of the morbid formations in question.]

Tubercle and Tuberculosis.

118. The structure characteristic of tuberculosis is the **tubercle**, or tuberculous nodule. The notion of tuberculosis is thus primarily an anatomical one—tuberculosis is a tubercular (*i.e.*, nodular) disease.

Of course it does not follow conversely—that every nodular growth found in the organism implies tuberculosis; the special nodule of tuberculosis, the tubercle *par excellence*, is a structure of definite and special constitution. Virchow ("Die krankhaften Geschwülste," ii., 636) describes a freshly formed tubercle as a small gray translucent nodule, not exceeding a millet-seed in size, mainly composed of cells, and developed from connective tissue. The cellular elements (he adds) are essentially similar to those of lymphatic glands; they are round cells of various sizes, some of them like white blood-cells, some larger, some smaller. Their nuclei are homogeneous and bright, small and spherical or large and oval, vesicular, and transparent; they contain nucleolar corpuscles. The larger cells often contain two nuclei, and frequently more, to the number of twelve or over. Between the cells are found fibrous filaments arranged in a network and sometimes vessels also. The latter are never

new-formed; they existed before the tubercle was developed, and lie within the tubercle only because the tubercle has grown around them. The nodules occur either singly or in numbers; or they may be grouped in confluent masses. In the latter case, the internodular tissue does not remain unchanged; it seems made up of imperfect granulation-tissue, or inflammatory fibrous hyperplasia takes place. The appearance is then rather that of a mass of compact uniformly diseased tissue, than of normal tissue containing nodular deposits.

When the nodule becomes older, the centre of it is invariably found to be caseated. It is then yellowish-white and opaque. Under the microscope it appears as a granular friable mass, while the periphery still shows its cellular constitution. The aggregations of cells may stretch out in various directions through the tissue, as if the nodule threw out pseudopodia.

The nodular groups undergo caseation like the single nodules. The internodular granulation-tissue also becomes cheesy, so that at length large and continuous caseous patches are formed. It is much rarer to find the nodules undergoing fibrous transformation. **Caseation** is characteristic of the later stages of the tuberculous nodule.

[The term tubercle (*tuberculum*) was formerly applied to all varieties of nodular growth. Baillie (1794) and Bayle (1810) were the first to direct attention to the gray miliary nodules which we now call tubercles. Bayle however applied the term to other growths in the lung. Laennec applied it mainly to the cheesy masses found in phthisical lungs. Larger caseous foci and caseous lobular infiltrations were also described as tuberculous. The caseous nodes and masses were simply "**tubercles,**" the diffused infiltration was "**tuberculous infiltration,**" the gray nodules (or true granulative tubercles) were "**miliary tubercles.**" Cheesy change was thus made the main characteristic of tuberculosis; caseation was spoken of as "tuberculization." In opposition to this view, Virchow maintained that caseous masses might arise in many different ways, and hence had very various significance in different cases. He laid it down that the anatomical basis of tuberculosis is the cellular tubercle (Virchow, *loc. cit.*; Waldenburg, "Die Tuberculose," Berlin, 1869; Grancher, "L'Union méd.," 1881).]

119. We may define a tubercle, then, as a non-vascular cellular nodule, which does not grow beyond a certain size, and at a certain stage of its development becomes caseous. This definition includes all that we can say, in general terms, of tubercle from the histological point of view. The histological researches of the last fifteen years (by Langhans, Schüppel, Köster, Rindfleisch, Cohnheim, Ziegler, Klein, Sanderson, and others) have added only this—that the tubercle possesses in many cases a special structure, and that certain cell-forms frequently occur in it and give it a characteristic appearance. The central part of the tubercle

usually contains **giant-cells** (Fig. 29, *a*). These possess numerous nuclei, which are not uncommonly arranged round the periphery, or gathered together at one pole of the cell. The uninuclear cells are partly lymphoid, partly larger and like swollen epithelial or endothelial cells—these are called **epithelioid** (Fig. 29, *b*). Giant-cells and epithelioid cells are marked by their coarsely granular protoplasm, and large vesicular oval nuclei with clear nuclear juice and nucleoli. The round or lymphoid cells (*c*) are finely granular, with a small round nucleus in which the nuclear juice and nuclear substance are not clearly distinguished.

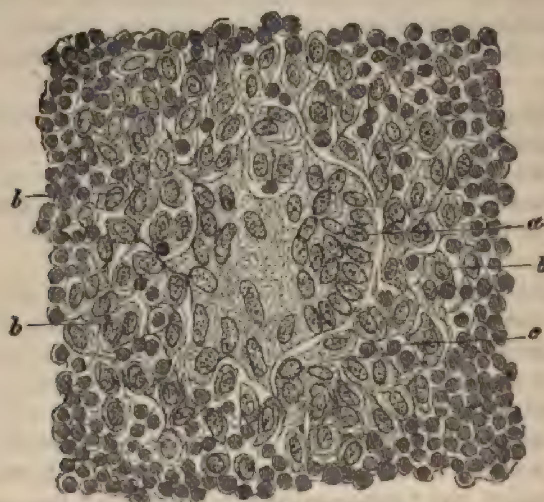

FIG. 29.—Tubercle from a Fungating Granuloma in Bone. × 250. (Aniline-brown staining.) *a*, giant-cell ; *b*, epithelioid cells ; *c*, lymphoid cells.

These cells lie in a stroma which in many cases exhibits a reticular arrangement.

120. The epitheloid cells and giant-cells have been thought by some to be characteristic of tuberculosis. Many writers have thus come to speak of specific tubercle-cells, and have based the diagnosis of tuberculosis merely on the presence of these larger varieties of cells. This is certainly unjustifiable. Such cells, indeed, are common enough in tuberculous affections, but they are by no means exclusively confined to them.

All inflammatory tissue-formation is preceded by a stage in which large cells are developed. It is very easy to generate experimentally in such formations all the various elements found in tubercle, and especially the giant-cells. The constituent cells of tubercle are precisely equivalent to the corresponding cells of granulation-tissue. All the evidence points to the conclusion that tubercles arise in the same way as granulations. The chief materials are derived from the migrated white blood-cells ; and the endothelial cells and fixed connective-tissue cells supply only a minor

part. So far as the cell-forms are concerned, the only difference between tubercle and granulation is—that in tubercle the larger cells are often found in relatively greater numbers.

The characteristic features of tubercle, therefore, do not lie in the forms of its cellular elements. As has been already said, the characteristic features are these: that the cells form a definite nodule, which does not exceed a certain size, contains no new-formed vessels, and in consequence at a certain stage of its development ceases to progress; that the nodule thereupon undergoes retrogressive changes, and becomes fatty, necrotic, and caseous.

If this proposition be duly considered, it will be seen that the diagnosis of tubercle cannot be made to depend on anatomical structure and constitution alone. A cellular nodule made up of round-cells only, without a single giant-cell, or a nodule whose general texture is fibrous, may perfectly well be characterized as a tubercle, if its life-history corresponds with what we have set down. As an actual fact, in perfectly typical cases of tuberculosis we may find such nodules close by others that contain giant-cells. We may explain the occurrence of the former, by supposing in the one case that the aggregated round-cells have prematurely ceased to develop or have not yet had time to reach their full development; in the other case the fibroblastic stage (that of epithelioid cells and giant-cells) has been exceptionally transcended, and that of fibrous-tissue formation has been reached. The physiological analogue of the last is of course the transformation of granulations into cicatricial tissue.

[According to the recent investigations of Koch (Art. 127), the definition of tubercle just given must be amended. By tubercle we are, it seems, in future to understand—a cellular nodule containing within it the specific tuberculous virus, the **Bacillus tuberculosis** of Koch.

The general doctrine of tuberculosis must be altered in many points in consequence of Koch's discovery. The text has been allowed to remain as representing the hitherto accepted doctrine, and as containing what is probably the truth, though not the whole truth.

Langhans was the first to examine carefully the giant-cells ("Virch. Arch.," vol. xlii.) and to describe their forms. Schüppel ("Untersuch. üb. d. Lymphdrüsentuberculose," Tübingen, 1871), maintained that they were always present in tuberculosis, and based the diagnosis of the affection upon them. Köster ("Virch. Arch.," vol. xlviii.), Buhl ("Die Lungenentzündung," Munich, 1872), and Rindfleisch ("Pathological Histology," i., 136, and "Ziemssen's Cyclopædia," vol. v.) have also insisted on their importance in diagnosis. The latter has even declared that any large-celled infiltration of a tissue is to be regarded as tuberculous or scrofulous in character. In opposition to this view Hering ("Stud. über Tuberculose," Berlin, 1873), has disputed the specific significance of giant-cells and epithelioid cells, and has demonstrated that they are often absent in undoubted tubercles. The second constituent

of the tubercle, the fibrous reticulum, has been investigated by Schüppel (*loc. cit.*), Wagner ("Das tuberkelähnliche Lymphadenom," Leipzig, 1871), Klein ("Report of Med. Officer of Privy Council," 1874). Cornil and Ranvier ("Man. of Path. Histology," vol. i., 1882), maintain that the reticulum is produced *post mortem* by the action of hardening reagents on the intercellular substance. For further references to the history of the question the student may consult Treves ("Scrofula and Tubercle," London, 1882), Hamilton (*Practitioner*, 1879–1881), Klein (*Practitioner*, 1881), Burdon Sanderson (*Practitioner*, 1882), Gee (Article "Tuberculosis:" "Quain's Dict. of Medicine," 1882).

Ziegler ("Ueber die Herkunft des Tuberkelelemente," Würzburg, 1875, and "Ueber path. Bindegewebsneubildung," 1876) has sought to show that neither giant-cells nor epithelioid cells are exclusively confined to tubercle, but are to be found in all granulations. Between the latter and tubercle the only difference is—that in healthy granulations the multinuclear cells occur but sparingly, while in tubercle they are in great numbers and highly developed. In tubercle the formative material is abundantly provided and fibroblasts produced, but they are not utilized for further development into fibrous tissue.

The giant-cells of granulation-tissue are to be distinguished from those which arise from epithelial cells. When tubercles form in epithelial ducts, such as those of the liver or testis, the affected epithelial cells seem to coalesce and form structures much resembling the giant-cells of granulations (cf. Klein, "Lymphatic System," part ii., London, 1875). They have properly nothing to do with the formation of the granulomatous tubercle. They are accidental consequences of the locality in which the tubercle is developed. To draw conclusions from them (as do Gaule, "Virch. Arch.," vol. xlix., and Lübimow, "Virch. Arch.," vol. lxxv.) with regard to the genesis of all tuberculous giant-cells is not permissible.]

121. **Diffusion of tubercle.** When a tuberculous organ is examined we do not usually find the tubercles in their earlier stages; they have already undergone certain advanced changes. Parenchymatous organs contain caseous nodulated patches or foci, which are either firm and compact in texture, or are already softened and broken down toward the centre. In surface-tissues, ulcerations are produced by this softening process, and their edges and base are caseous. The caseated tissue passes at its boundaries into a zone of gray or grayish-red translucent tissue, reminding one exactly of granulation-tissue. This gray or grayish-red tissue is found in other parts of the affected organ in the form of larger or smaller patches; these often quite visibly contain small gray or yellowish white and opaque nodules.

Lastly, the affected organ also contains small gray nodules lying in apparently unaltered tissue; and sometimes surrounded by a hyperæmic zone, sometimes not.

The gray or grayish-red translucent tissue, whether it surrounds the

caseous focus, or forms the base of an ulcer (Fig. 31, *h* and h_1), or occurs in isolated patches, is nothing else but tissue infiltrated with cells; it is granulation-tissue. The gray and the yellow nodules are fresh or "crude" tubercles generally containing giant-cells (Fig. 30, *f*), and old already caseated tubercles (Fig. 31, i_1), respectively. The gray and yellow isolated or aggregated nodules in the neighborhood of the larger patches are of the same character (Fig. 30, *g*, and Fig. 31, *i* and i_1).

From these observations we may gather—that tubercles sometimes

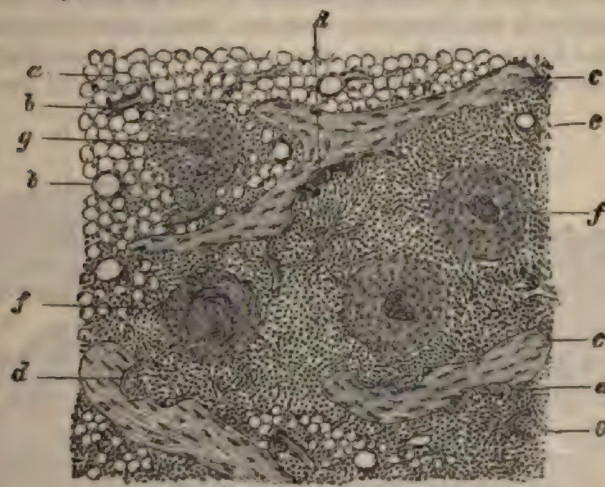

FIG. 30—Fungating Granuloma with Tubercles from the Calcaneum. × 60. (Hæmatoxylin staining.) *a*, medullary tissue containing fat; *b*, blood-vessels; *c*, bone trabeculæ; *d*, osteoclasts (Art. 115); *e*, granulation-tissue; *f*, tubercles in the granulation-tissue, some containing giant-cells; *g*, isolated tubercle.

occur aggregated or grouped within a tissue which is already infiltrated with cells; and that the affection spreads by the formation of fresh nodules in the neighborhood of the old. In other cases granulation-tissue and fibrous tissue may develop between and around the aggregated tubercles. The process may thus begin with an eruption of tubercles, or with a more diffused inflammatory infiltration. These propositions practically include all that is important concerning the diffusion of tubercle in the tissues.

[It is not usually difficult to recognize tubercles in the substance of tuberculous granulation-tissue. The giant-cells and epithelioid cells seen in microscopical sections do not take color nearly so well as the small round-cells which form the main component of the tissue. Three zones are usually distinguishable in a tubercle. In the centre lies the core of aggregated giant-cells of a dark or dull color. Then comes the zone of faintly stained epithelioid cells, and finally at the periphery the zone of deeply stained round-cells; these last are usually deeper in tint than the granulation-cells around them. When the middle of the tubercle has

already become caseous, giant-cells are generally to be made out here and there over it.

It is not always correct to say that tuberculous patches take their rise from single nodules. The formation of nodules may be preceded by a diffused infiltration, or even the development of granulation-tissue; the nodules only making their appearance as secondary growths.]

122. The eruption of fresh tubercles in the neighborhood of an existing tuberculous focus is usually followed sooner or later by the appearance of nodules in the lymphatic system. The nearest lymphatics are, of course, the first to be affected; they receive their lymph from the region primarily affected. Thus in tuberculous ulceration of the mucous

FIG. 31.—Subepithelial Tuberculous Granulations and Discrete Tubercles in the Wall of the Large Intestine. × 30. (Bismark-brown staining.) *a*, mucosa; *b*, submucosa; *c*, muscularis interna; *d*, muscularis externa; *e*, serosa; *f*, solitary gland; *g*, mucosa infiltrated with cells; *h*, tuberculous ulcer; h_1, focus of softening or tuberculous abscess; *i*, "crude" or fresh tubercle; i_1, caseous tubercle.

and submucous coats of the intestine, first the lymphatics of the muscular coats (Fig. 31, *c*, *d*) are infected, and then those of the serous coat. In this way strings of tubercles may be formed along the course of the vessels.

From the nearer lymphatics the eruption may pass in succession to others, and at length approach the thoracic duct. More frequently the affection is not uniformly diffused in this way, but attacks certain parts of the lymphatic system rather than others, especially those through which the lymph is as it were filtered, namely the lymphatic glands.

It is in the glands that the tuberculous eruption is most intense. Generally the process makes a kind of halt at these gland-stations; but it sooner or later finds opportunity to spread onward, and at length reaches the main trunks and the thoracic duct itself.

Wherever the tuberculous process has become established, it is distinguished by the development of tubercles, and this in the lymphatic vessels as well as the glands (Fig. 32).

A more or less intense inflammation of the surrounding tissue is always associated with the tubercular eruption ; it is manifested by hyperæmia with infiltration and swelling. If the process last for a certain time, it not infrequently happens that young connective tissue is developed at the seat of the eruption. The usual fate of the tuberculous growth is caseous necrosis and disintegration. It rarely issues in the formation of fibrous tissue, and still more rarely in complete resorption of the tubercle.

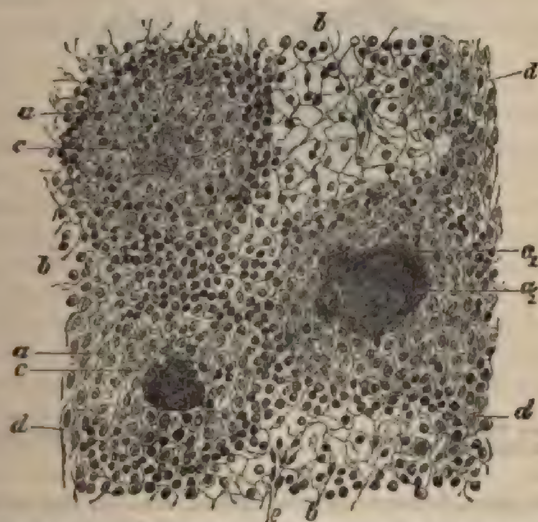

FIG. 32.—Tuberculosis of a Lymphatic Gland. × 150. (Hæmatoxylin staining.) a, large-celled tubercle with giant-cell (c); a_1, tubercle with central caseation and giant-cells (c_1); d, epithelioid cells lying outside the tubercles in the adenoid reticulum (b) of the gland ; e, lymphoid cells.

123. The virus which engenders tubercle may be carried out of the lymphatic system into the blood, either from a tuberculous focus in a gland or a tuberculous ulcer in the thoracic duct. It may thus be conveyed to distant organs. This will also happen when the virus passes directly from a tuberculous focus into an artery or vein. The result is an eruption of new tubercles either local or general.

When the infection of the blood results in a general eruption of tubercles throughout all the organs or in most of them, the affection is called **acute miliary tuberculosis.** The various organs are beset more or less densely with minute (miliary) gray or translucent nodules, or here and there with yellowish-white opaque nodules with cheesy centres. This is the case whether the affection extend to several organs or to one, or even to a single arterial territory within an organ.

All these nodules are made up of cells. In their earliest stages they

are nothing but little heaps of small round-cells (Fig. 33, *b*), unquestionably derived from the blood. Many foci maintain this character until they are mature; all the cells do is to multiply. In other cases giant-cells and epithelioid cells (Fig. 32, *a*) are developed. In these cases, as in the others, the nodule ultimately becomes caseous. Very seldom does fibrous transformation or resorption occur.

Diffused and wide-spread inflammatory disturbance of the circulation is very often associated with the eruption of the nodules. This is especially the case in the pia mater, the serous membranes, and in the lungs, where the process is often accompanied by copious and diffuse exuda-

FIG. 33.—Miliary Tuberculosis of the Liver. (Carmine staining.) *a*, mature tubercle in the portal sheath; *b*, tubercle beginning to develop in a liver-cell.

tion. In the liver, kidney, thyroid gland, etc., on the other hand, the changes elsewhere than in the immediate neighborhood of the nodules are usually but slight.

[Ziegler has investigated the development of miliary tubercles occurring in very diverse structures, and maintains that their basis is always a collection of white blood-cells which have migrated from the veins and capillaries. These indeed often form the entire mass of the tubercle. In other cases the endothelia contribute something. When the nodule has reached a certain size it becomes difficult to make out certainly the behavior of the fixed cells of the tissues. He has not been able to confirm the often-made assertion that miliary tubercle is specially apt to develop round the smaller arteries.

The direct penetration of the tuberculous virus into the blood-vessels may be the result of tuberculous change in their walls. If a considerable number of sections of phthisical lung be examined, there will here and there be found vessels whose walls are the seat of tubercles. If these penetrate the intima, they may then break into the blood-channel

directly. Weigert has shown that large venous trunks may be invaded in this way.

There are two reasons for the fact that all organs are not simultaneously and equally attacked when the blood is infected with the tuberculous virus. One is that the virus, though it is circulating in the blood, may not reach all the organs alike. The other is that all the organs are not equally predisposed to infection. The skin, for instance, seems to enjoy almost perfect immunity.

General miliary tuberculosis is not an inevitable result of tuberculosis occurring in an organ. The rule rather is that the tuberculous process does not extend beyond the boundaries of the organ primarily affected, and the lymphatic glands pertaining to it. What most commonly leads to general infection of the blood is the disintegration of caseous tuberculous glands.]

124. Tubercle may be disseminated in other ways, and independently of the lymphatics and blood-vessels. Consider, for example, the mode in which it spreads on the surface of mucous membranes. It is easy to verify that solitary nodules, as well as tuberculous patches and ulcers of larger size developed in mucous membrane, do not long remain isolated, but soon give rise to new foci. These are situated not merely in the immediate neighborhood of the first, but often at a considerable distance from them. They may even appear unconnected with the first lesions; while it is certain that they are not, at least in every case, propagated through the lymphatics. In pulmonary tuberculosis, for instance, which has already passed into the ulcerative stage, it is not at all uncommon for the mucous membrane of the air-tubes to become affected. This is especially apt to occur in the larynx, epiglottis, and at times in the pharynx; and the affection often extends to the lower segments of the large and small intestines. When the kidneys become tuberculous, and contain caseous ulcerations, the ureters, bladder, seminal vesicles, and prostate may become consecutively diseased. In other cases the process commences in the latter organs and extends upward.

From such instances it becomes plain that the infective virus may actually be transported along the surface of the mucous membrane. It attacks the spots at which it is allowed to linger, and penetrates the mucous tissue. It there sets up the specific inflammation manifested by the development of nodules, which disintegrate and produce ulcerations.

Tubercle is in like manner disseminated on the surface of the serous membranes lining the great body-cavities. In their case it is obvious that the transport of the virus is favored by the normal movements and displacements of the contained organs.

[It must be remembered, in connection with this question, that all mucous membranes are not equally susceptible with regard to the tuberculous virus. The mucous membrane of the mouth, pharynx, and œso-

phagus is far less susceptible than that of the larynx and trachea. The stomach, duodenum, and bile-ducts, as also the urethra, are very rarely attacked. This is explicable now that we know that the virus is a special micro-organism (Art. 127); for the secretions of the stomach, duodenum, and common bile-duct are prejudicial to the development of bacteria. The œsophagus and urethra have this advantage—that they are continually being swept clean, as it were. In the small and in the large intestine, where the process of absorption goes on most actively, the ingesta and with them any tuberculous sputa which may happen to have been swallowed, may lie a long time in contact with the mucous membrane. In the neighborhood of the larynx, the bronchial secretion continually accumulates before it is coughed out, and the virus has thus abundant opportunity of attacking its mucous membrane. The bladder, in like manner, contains the accumulating secretion of the kidneys, while the urethra is only "flushed" with it from time to time. In addition to these factors, however, we must not leave out of account the possibility of special predisposition in the various structures and tissues.]

125. **The clinical significance of tubercle.** The processes just described (Arts. 118–124) are comprehended under the term tuberculosis. Tuberculosis, so defined, is distinguished by two chief characters. The one is anatomical, namely, the development of specific nodules; the other is clinical, namely, the consecutive invasion of one or more parts of an organ or of the entire system.

As a disease, tuberculosis is distinguished by its progressively destructive tendency. It not only destroys gradually the organ first attacked, but it seizes by various routes upon other organs, or spreads throughout the organism.

In addition to this clinical characteristic of progressive invasion, we have the anatomical characteristic—the tubercle. Tuberculosis is anatomically an inflammatory process; but its course does not correspond with that of other inflammations. It is sharply distinguished from them by the development of nodules both in its original seat and in the parts that are secondarily attacked; and these nodules have a definite type and structure—they are cellular and non-vascular.

There is still another characteristic, but we owe our knowledge of it not so much to observation at the bedside or at the post-mortem table, as to direct experiment. Villemin and Klebs were the first to show—what many investigators (such as Waldenburg, Cohnheim, Orth, Bollinger, Simon, Wilson Fox, Klein, and Burdon Sanderson) have since verified—that tuberculosis is transmissible to animals. In other words, when animals are inoculated with matter from fresh or caseous tuberculous foci, they are forthwith attacked by a disease which, judging from its clinical course and anatomical products, is identical with human tuberculosis.

This character determines the genus of tuberculosis in the classification of human diseases. It is an infective disease.

[The proposition that tuberculosis is anatomically an inflammatory process is disputed by many pathologists. There has always been a strong inclination to reckon tubercle among the true tumor-formations, like cancer. Such a view will hardly be maintained now. The genesis of tubercle, its cellular constitution, its whole life-history, are all in favor of its kindred with the inflammatory new-formations; they offer no fair grounds for comparing it with the tumors. We may add that the possibility of generating tubercles by inoculation with caseous or necrotic tuberculous matter is a strong argument for regarding tubercle not as a tumor but as a product of inflammation.

The fact of the transmissibility of tuberculosis to animals is now placed beyond doubt. It is true that the experiment does not always succeed; for though some animals are very susceptible, such as rabbits, guinea-pigs, and ruminants generally, others, like dogs, enjoy a certain degree of immunity. This only proves, not that tuberculosis is not infective, but that the tuberculous virus is not a universal poison, capable of attacking each and every organism. This is likewise the explanation of the fact that physicians have observed comparatively few cases of quite indubitable transmission of the disease from man to man. Among human beings there are predispositions; tuberculosis does not attack all with equal readiness. Nor must we forget, in criticising the clinical data, that it is scarcely possible to discern the exact time at which tuberculosis sets in. The clinical manifestations may not appear till long after the first infection, when it is impossible to make out anything that throws light on the origin of the disease (Budd, *Lancet*, 2, 1867; Weber, "Clin. Soc. Trans.," 1874; Rindfleisch, "Virch. Arch.," vol. lxxxv.; Burney Yeo, "Contagiousness of Pulm. Consumption," London, 1882).

A short but very comprehensive summary of the evidence for the transmissibility of tuberculosis from man to man, and from man to lower animals, is given by Klein (*Practitioner*, August, 1881). The student who desires to know the "state of the case" for the specific nature of tuberculosis immediately before Koch's discovery cannot do better than to consult this article.

Inoculation experiments have been made in various ways. The tuberculous matter has been inserted under the skin, into the peritoneal cavity, into the eye, and into the joints; it has been mixed with the food; it has been pulverized and conveyed to the lungs with the respired air.

References:—Villemin, "Gaz. hebd.," 50, 1865; "Comp. Rend.," 61, 1866; "Études sur la tuberculose," 1868; Lebert, "Bullet. de l'acad.," xxxii.; "Gaz. méd. de Paris," 25–29, 1867; Lebert and Wyss, "Virch. Arch.," vols. xl. and xli.; Roustan, "L'inoculabilité de la Phthisie," Paris, 1867; Feltz, "Gaz. méd. de Strasbourg," 1867; Wilson Fox, "The artificial production of Tubercle," London, 1868; Chauveau, "Gaz. méd. de Lyon," 1868; Langhans, "Die Uebertr. der Tuberculose auf Kaninchen," 1868; Waldenburg, "Die Tuberculose," Berlin, 1869; Vir-

chow and Hirsch, "Virch. Jahresber.," 1868–1870 (containing full and very useful references to previous research); "Trans. Path. Soc.," 1873 (an instructive discussion of current views); Klebs, "Virch. Arch.," vols. xliv., xlix.; "Arch. f. exp. Path.," i.; "Naturforscher-versammlung in München," 1877; Cohnheim and Fraenkel, "Virch. Arch.," vol. xlv.; "Die Tuberculose vom Standpunkte der Infectionslehre," Leipzig, 1880; Klein, "Lymphatic System," ii., London, 1875; Tappeiner, Lippl, Schweninger, "Naturf.-versamm.," 1877; Tappeiner, "Virch. Arch.," vol. lxxiv.; Orth, "Virch. Arch.," vol. lxxvi.; Bollinger, "Arch. f. exp. Path.," i.; H. Martin, "Recherches sur le tubercule," Paris, 1879; "Arch. de Physiologie," 1881; "Revue de méd.," April, 1882; Sanderson, "Report to Med. Off. of Privy Council," 1868–69 (republished in *Practitioner*, September to December, 1882; a critical summary of preceding researches is given in the latter of these reports); Kiener and others, "L'Union méd.," 1881.]

126. Two important questions remain unanswered. Tuberculosis is an infective disease; and it bears the anatomical character of a destructive nodular inflammation. It is important for diagnostic purposes to know something more. Does the tuberculous inflammatory process manifest itself by the formation of nodules only? Conversely, are all varieties of cellular nodules, exhibiting the general structure of tubercles, to be regarded as evidence of tuberculosis? The second question is—What is the nature of the tuberculous virus? In answer to the former question, clinical observation and experiments on animals have shown that all nodular eruptions are not tuberculous. Thus when small irritating foreign bodies are introduced into the body of an animal, it sometimes happens that a nodular affection is produced which anatomically simulates tuberculosis. Yet these nodules have in reality no kindred with true tubercles. The exciting cause is essentially different (Art. 127) from that which engenders true tuberculosis; while neither the life-history of the nodules, nor the course of the process as a whole, corresponds with what is observed in human tuberculosis.

Moreover, there occur in man certain nodular inflammations whose clinical course is radically different from that of tuberculosis, though the nodules in some degree resemble tubercles. The best known instance is lupus of the skin (Art. 132). In this affection perfectly typical tubercles are frequently formed; but they never induce tuberculosis in other organs, or general tuberculosis. In the peritoneum, again, there are now and then found tuberculoid nodules; but they have probably nothing whatever to do with tuberculosis as a disease.

While the domain of tubercular eruptions is on one hand somewhat wider than that of tuberculosis, on the other hand the domain of tuberculosis goes beyond that of tubercular eruptions. In other words, there may be tuberculosis without isolated tubercles. It not infrequently happens that in the course of tuberculous disease inflammatory patches are

formed, consisting of diffuse continuous granulations in which no tubercles can be detected. These patches must nevertheless be acknowledged to be tuberculous ; the clinical course of the process, and the life-history of the new inflammatory tissue, indicate this ; while tubercles may actually be developed in later stages of the same affection. In such cases it may be hard to determine whether the process is really tuberculous ; especially in organs like the lungs, where the usual inflammatory changes are at all times apt to make the recognition of tubercle a difficult matter. Experimental inoculation, or the detection of the specific virus (Art. 127), can alone settle the question. As regards the latter test we may expect that the near future will bring us much additional information. It is fortunate that these ambiguous cases are not very numerous. Although, therefore, the anatomical notion of tubercle and the clinical notion of tuberculosis do not precisely correspond throughout their full extension, they do correspond in the vast majority of cases. It is a rule almost without exception, that tuberculosis is distinguished microscopically and on the post-mortem table by the presence of tubercles.

[Much confusion has arisen in the discussions on tuberculosis from the assumption that the production of a nodular or tubercular eruption in an animal is necessarily the same as the production of tuberculosis. The result of the assumption has been that observers have fancied they have induced tuberculosis in animals by the introduction of all sorts of foreign bodies. The diagnosis is not to be based on the presence of nodules simply ; the life-history of the nodules and the general course of the whole process are also of essential importance (H. Martin, "Arch. de Phys.," 1881).]

127. We are now able to give a definite answer to the second question raised in the last article—What is the nature of the tuberculous virus?

At the meeting of the Berlin Physiological Society held on March 24, 1882, Dr. R. Koch communicated some result of his researches on tuberculosis, which constituted a distinct advance in our knowledge of its etiology.

He announced that the tuberculous virus is a special bacillus (**Bacillus tuberculosis**, Art. 206). Its length is about a third of the diameter of a red blood-cell, and its breadth one-fifth to one-sixth of its length. Individual bacilli contain clear bright spores. The bacilli are chiefly found in fresh tubercles, more sparingly in older ones. Some of them lie within the cells and especially within the giant-cells, others lie outside. They are generally single and scattered ; at times they are found in prettily grouped clusters. By treatment with methylene-blue and vesuvin, they take up a different tint from that of the surrounding tissues. The tissues stained in the first instance with methylene-blue have their color discharged by vesuvin, while the tubercle-bacilli retain it.

[Ehrlich, Gibbes, and others (*Brit. Med. Journ.*, October 14, 1882) have devised simpler and speedier methods than Koch's for staining, and so detecting the bacilli. These methods are readily applicable to the clinical examination of phthisical sputa.]

Koch has shown that the bacilli may be cultivated in the serum of ox-blood. The bacilli so bred may then be introduced into the bodies of various animals, such as rabbits, rats, and dogs, and tuberculosis is thereupon induced; in other words, they are attacked by a disease characterized by a progressive formation of cellular nodules. The nodules always contain the characteristic bacilli. In guinea-pigs the first appearance of disease is manifested ten days after inoculation.

It may therefore be accepted as an established fact that tuberculosis is an infective disease, induced by the presence of a specific bacillus.

In the light of this knowledge, the various theories which have been advanced with regard to the causation of tuberculosis become in some respects irrelevant. It will be matter for further experimental investigation to determine the vital properties of the tubercle-bacillus. Among other points, it will have to be settled whether the bacillus can develop only within the bodies of men and other mammals, or whether it may not pass through some stage of its existence outside the body; in other words, whether the disease is strictly contagious, *i.e.*, transmissible directly from one subject to another; or whether it is due to something of the nature of a miasma—a poison which may develop outside the body. According to Koch, the bacillus can only be bred between the temperatures of 30° C. and 41° C. (86° F.—105.8° F.). If this be so, it is hard to see how it can multiply outside the body. With regard to the transmission of tuberculosis from animals to man, it is to be noted that Koch has found the specific bacillus in the nodular growths which occur in the "pearly disease" of cattle (*Perlsucht*, or bovine tuberculosis).

Clinical experience would seem to indicate that the tubercle-bacillus is no ordinary bacterium, such as may enter and affect any organism without distinction. It would seem rather as if infection occurred only where a definite predisposition exists, or where a considerable quantity of the virus is introduced. This predisposition may be local as well as general. The local predisposition may perhaps depend mainly on antecedent inflammatory change. A general predisposition is attributed to **scrofulous** subjects especially. These are persons whose tissues exhibit a certain frailty or susceptibility to injury, that makes them particularly liable to chronic inflammatory disorders. It is, however, not at all uncommon for the term "scrofulous" to be applied to individuals actually affected with tuberculosis, as well as to those who are only predisposed to it.

We may imagine the course of the infection to be this: The bacilli settle in a tissue accessible from without, pass thence into the deeper structures, and ultimately into the blood; or, without any primary local

settlement, they may be taken up by the circulating juices directly, and carried to various parts; wherever they settle they begin to develop, and so set up inflammation and the formation of cellular nodules.

[Koch has found the bacillus not only in general miliary tuberculosis but in caseous pneumonia, caseous bronchitis, intestinal and glandular tuberculosis, "pearly disease," spontaneous and inoculated tuberculosis in various animals, and in the so-called scrofulous hyperplasia of lymphatic glands. All these affections are thus to be included under the head of tuberculosis; they are all the result of the same bacterial infection. Tuberculosis, from this point of view, is an infective disease not always manifested by the formation of tubercles. It may even appear as a purely local affection, and yet be unaccompanied by tubercles.

If is of special interest to note that Koch has detected the bacillus in the sputa of phthisical patients. As the bacillus produces spores within the body, it is very likely that the virus exists and diffuses itself outside the body mainly in the form of spores.

Koch finds that the bacilli grow very slowly, and after inoculation proceed to develop and multiply only when they reach a spot where they are not subject to much mechanical disturbance or displacement. From this we may understand how it happens that many persons, though again and again exposed to the invasion of tubercle-bacilli, yet remain uninfected. It is, moreover, conceivable that individuals in whose tissues inflammatory changes have already occurred are those who are most disposed to tuberculous infection.

At the time when Koch was bringing his researches to an end, Baumgarten ("Centralblatt f. d. med. Wiss.," 15, 1881) succeeded in detecting bacilli in tubercle by treating microscopic sections with dilute solution of caustic potash. He did not, however, go on to cultivate and inoculate the bacilli. Aufrecht had already described bacilli which he had found in tubercle ("Path. Mitth.," Magdeburg, 1881); but his demonstration was likewise defective. He did not show that the bacilli were peculiar and specific as regards tuberculosis.

It has been a much-debated question whether or not human tuberculosis is identical with the bovine "pearly disease." Anatomically the pearly disease is a progressively advancing affection in which nodes and nodules are formed. These may be single or agglomerated into masses as big as a potato. They are chiefly found in the serous membranes, as also in the lymphatic glands, lungs, and liver. In the serous membranes, the nodular masses are often pedunculated and pendulous. Caseation is not very common; calcification much more so. The nodules are essentially cellular in structure, often contain giant-cells (Virchow, "Virch. Arch.," vol. xiv.), look very like tubercles, and may lie together in great numbers in the midst of a cellular stroma.

A. C. Gerlach ("Jahresb. d. k. Thierarzneischule in Hannover," 1869) fed and inoculated rabbits and goats with matter from such nodules, and

on the strength of his experiments maintains that the pearly disease is transmissible to other animals and is identical with human tuberculosis. Schüppel ("Virch. Arch.," vol. lvi.) and Creighton ("Bovine Tuberculosis in Man," London, 1881), from microscopic comparison of tubercles and the pearly nodules, declare that they are identical. Orth ("Virch. Arch.," vol. lxxvi.) arrived at the same conviction through experiments in which the animal was fed with the infective matter; as did also Bollinger and Klebs ("Arch. f. exp. Path.," i.), Chauveau ("Jahrb. der. ges. Med.," 1872), and Baumgarten ("Berl. klin. Woch.," 49, 1880). On the other hand, Colin ("Compt. Rend., 1876), Günther, Harms, and Müller ("Jahrb. der ges. Med.," 1873–74) obtained only negative results. Virchow ("Berl. klin. Woch.," 1880, and "Virch. Arch.," vol. lxxxiii.) also made experiments by the method of feeding, but his results were ambiguous. He thinks that, so far as experiments have hitherto gone, the transmissibility of the pearly disease to other animals (by feeding them with diseased milk or meat) is not yet certainly established.

Koch's observation of the specific bacillus in the pearly nodules seems to remove all doubt of their identity with tubercles. How far the bovine disease may be transmitted to man is not yet made out. The transmission is at any rate possible, and that by various channels.]

Syphilis.

128. **Syphilis** is an infective disease, originating in a fixed contagium. It starts at a wounded or abraded spot, gives rise there to certain local tissue-changes, and thence spreads through the entire system. The poison of syphilis occurs in the human organism only; it is nowhere reproduced but within the human organism; and it is conveyed to other individuals only by direct transference. When transplanted into a new organism, it excites inflammatory processes of the most diverse intensity and extent—from simple localized and transitory hyperæmia to the formation of enormous exudations, or granulomatous growths, or extensive fibrous hyperplasias. If a child be procreated while the infection lasts, the disease may be transmitted to it from the mother's side as well as from the father's.

The primary inflammatory focus is formed at the seat of infection as an **indurated chancre** or "hard sore." It is an ulcer with an hardened bacon-like or gristly base and margin. It generally begins as an excoriation, *i.e.*, a slight and superficial loss of substance, and over this a vesicle or pustule is formed. In other cases it is developed from a node formed (for example) in the scar of a former ulcer; this then breaks, giving rise to the characteristic ulcer with its hardened gristly base. In other cases again the ulcer is first formed, and the induration follows later on.

The node or induration which forms the **primary lesion** of syphilis appears under the microscope at first as a dense infiltration of the connective-tissue with small cells (Fig. 34, *a*). The process may not advance

beyond this ; but in many cases the infiltrating cells proceed to develop further. From the small round-cells larger formative cells (Fig. 34, *b*), and not infrequently giant-cells (*c*), are formed. The development does not advance beyond this point ; the greater part of the affected tissue breaks down and ulcerates, or is reabsorbed. Some part of the cells go to form a cicatrix.

[Nothing certain is known concerning the nature of the syphilitic virus. Klebs ("Arch. f. exp. Path.," x.) regards the disease as a parasitic bacterial affection. Our histological knowledge of syphilitic growths

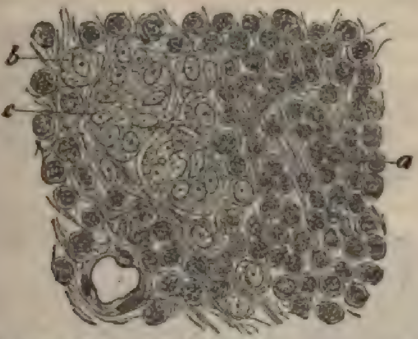

FIG. 34.—Section of a Syphilitic Hard Sore. × 350. (*Alum-carmine preparation.*) *a*, infiltration with round-cells ; *b*, large uninuclear ; *c*, multinuclear, formative cells.

is mainly due to Virchow ("Krank. Geschwülste," ii.), E. Wagner ("Arch. d. Heilk.," iv., 1863), Auspitz and Unna ("Vierteljahrsschr. f. Derm. und Syph.," iv., 1877). See also Baumler, "Ziemssen's Cyclopædia," vol. iii. ; Van Oordt, "Des tumeurs gommeuses," In. Diss., Paris, 1859 ; Cornil and Ranvier, "Man. of Path. Hist.," vol. i.]

129. After a certain time the "initial sclerosis" or hard sore is followed by inflammations of the lymphatic glands, skin, and mucous membrane. These are the **"secondary symptoms."** Still later appear syphilitic inflammations of the viscera and bones. These are the **"tertiary symptoms."** The various inflammations are for the most part similar to other, non-syphilitic, inflammations. Certain special granulomatous formations are also developed which are called syphilomata (Wagner) or gummata, and condylomata.

The syphilitic **condyloma** (*condyloma latum* or **mucous patch**) is a raised level patch on the skin or mucous membrane, due to inflammatory change in the epidermis and corium, or in the epithelium. The upper layers of the corium, and especially the papillæ, swell up greatly owing to infiltrations of cells and liquid exudations. The cutis appears as a loose sodden gelatinous tissue infiltrated with cells (Fig. 35, *i* and *k*). There is no true granulation-tissue as a rule, for no organization of the cellular material takes place, and no new vessels are formed. In condylomata of the mucous membranes, the tissue may take on something of

the look of granulations owing to abundant cell-production. The epithelium is usually swollen (Fig. 35, *e*, *f*, *g*) and infiltrated with cellular and liquid exudations.

The syphilitic **gumma** in its earlier stages is histologically very similar to the condyloma. The gumma is a circumscribed patch of morbid tissue, not unlike granulation-tissue. It occurs chiefly in the periosteum, muscles, brain-substance, and membranes, as well as in the parenchymatous organs of the abdomen, such as the liver, spleen, and testis.

FIG. 35.—Condyloma Latum Ani, or "Mucous Patch." × 100. (Aniline-brown staining.) *a*, horny layer; *b*, rete Malpighii; *c*, corium; *d*, loosened horny layer infiltrated with leucocytes; *e*, rete Malpighii swollen and (*f*) infiltrated with cells; *g*, degenerate epithelial cells containing leucocytes; *h*, granular coagula; *i*, papilla swollen and infiltrated with cells and exuded liquid; *k*, corium infiltrated with cells, exuded liquid, and coagula; *l*, lymphatic distended with coagula; *m*, sweat-gland.

The relative proportion of cells in the gumma varies with its site. Varieties which are poor in cells, such as are found at times in bone, are soft and gummy in texture. On section they have a gelatinous look, the liquid constituents exceeding the cellular in quantity. The older surrounding tissue undergoes in part a mucoid change. Varieties rich in cells, met with chiefly in the pia mater and arachnoid, and the spleen, form nodes or patches which are translucent, gray or whitish, or grayish-red in color, and rounded (spleen) or irregular (brain-membranes) in shape. They have in fact the exact appearance of granulations. In the affected organs or tissues there are usually found, in addition to the gummata, more diffused and extensive inflammatory changes.

130. These syphilitic granulomatous growths are generally of a very perishable or unstable nature. Frequently there is no proper granulation-tissue developed ; that is to say, no vessels are formed and no further development of the extravasated leucocytes takes place. The leucocytes usually perish by fatty degeneration. Small infiltrated patches may often disappear by reabsorption. In other cases, as in the bones, suppuration or fatty necrosis and ulceration is the issue. In larger patches abounding in cells, caseous nodes are not infrequently formed ; they may be either rounded and spherical or irregular in shape. If the caseous process is still in a comparatively early stage, these patches are found surrounded by highly cellular granulations. After a time these latter pass into dense fibrous tissue (Fig. 36), and contract into a narrow zone surrounding the caseous patch. Lastly, this zone may be further transformed into connective tissue of a more ordinary type. Caseous nodes, thus imbedded in an irregular puckered capsule of scar-tissue, are found most commonly in the liver and testis.

It is these scar-surrounded caseous nodes which are chiefly referred to when **gummatous nodes** are spoken of. They have of course ceased

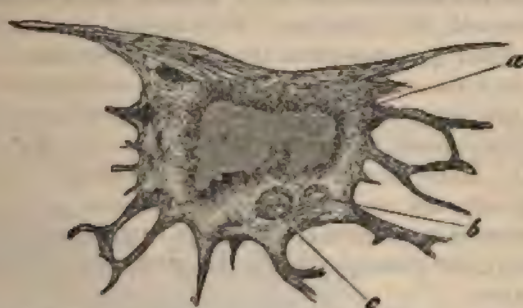

FIG. 36.—Gumma of the Liver undergoing Caseation. + 25. *a*, gumma enclosed in an irregular capsule of scar-tissue ; *b*, artery with thickened wall ; *c*, obliterated portal vein.

to be strictly gummatous, for they contain merely the caseous detritus of the original cellular gumma. The caseous change often involves not merely the cellular new-formation, but also the normal tissue of the affected organ. The node comes thus to contain more than the necrotic remains of the true gumma ; it includes all or most of the proper or specific tissue affected and destroyed by the original infiltration.

This common issue of syphilitic inflammation in disintegration and necrosis seems to depend chiefly on the nature of the virus which produces the disease. It is not, however, impossible that another factor may lie in the aptness of the vessels and especially the arteries to be attacked by the specific inflammation. Wherever granulations are formed or hyperplasia set up in consequence of syphilitic inflammation, the vessel-walls and chiefly the intima are observed to thicken. The lumen is thus narrowed, and often entirely occluded (Fig. 36, *b* and *c*, and Art. 297).

[On syphilitic disease of the arteries see Greenfield, etc., "Trans. Path. Soc.," vol. xxviii.; Heubner, "Die luetische Erkrankung der Gehirnarterien," Leipzig, 1874; Lancereaux, "Gaz. des Hôp.," 21, 1876.]

Leprosy.

131. **Leprosy,** lepra or *elephantiasis græcorum*, is a disease distinguished anatomically by the formation of nodes and tubers in the tissues. These, when cutaneous, are usually seated on the surfaces exposed to the air—the face, hands, and feet. They may at times occur elsewhere. The subcutaneous tissues, nerves, mucous membranes, and viscera may also be affected. The nodes may reach the size of a walnut.

When a node is about to form in the skin, there appears first a red spot, which becomes bluish and then brown; the underlying tissue becomes meanwhile thickened and indurated. The swelling then increases, and the patch becomes gradually transformed to a firm red protuberance, which later on becomes softer and paler.

The basis of the node is made up of cellular granulation-tissue, lying immediately beneath the epidermis. It is spread in a uniform layer, or sends down cellular processes into the deeper structures. In color it is grayish-white and somewhat translucent. The cells are of various sizes according to their stage of development. When the nodes break down, leprous ulcers are formed, though these are more commonly the result of external injury. Fatty metamorphosis of the cells and resolution of the tumor thereby are not unknown, but the process is very slow. The nodes of the mucous membrane are more apt to ulcerate than those of the skin; this occurs, for example, inside the nose, and in the conjunctiva, mouth, and larynx.

Leprous growths in the nerve-sheaths may lead to disturbance of the nerve-functions; we may thus have local amyotrophy and anæsthesia, as in Lepra anæsthetica. Visceral leprosy is rare.

Armauer Hansen and Neisser have discovered that leprosy depends on the presence of a specific bacillus (**Bacillus lepræ**) in the affected tissue. The bacillus is found in all leprous foci (Neisser), generally enclosed in the larger cells. The hereditariness of leprosy has not been proved. It is but slightly contagious; yet in certain regions it is endemic. It is nowadays rare in Europe; Norway and Sweden, Finland, and the Baltic provinces of Russia, are the regions where it is most prevalent. It occurs (but more rarely) in special districts of Greece and Italy. It is prevalent in Central and South America, and in Southern Africa and Asia.

[Virchow's "Onkologie" (vol. ii.) contains a full account of leprosy, from which the above details are chiefly drawn. Thoma ("Virch. Arch.," vol. lvii.) gives a description of the histological characters of the disease

agreeing in essence with Virchow's. Neisser's discovery of the *Bacillus lepræ* was announced in the "Breslau. ärzt. Zeitschrift," 20 and 21, 1879; Armauer Hansen's in "Virch. Arch.," vol. lxxix. See also Neisser, "Virch. Arch.," vol. lxxxiv. The bacilli have been found in the nodes of the skin, oral epithelium, and larynx—as well as in diseased foci in the nerves, cartilages, testes, lymphatic glands, liver, and spleen. Neisser has inoculated rabbits and dogs with leprous matter, and so produced inflammatory nodes corresponding with those of human leprosy. He supposes that the bacilli enter the system as spores, and develop wherever they find a suitable nidus, especially in the lymphatic glands. Thence they invade the entire body.

Köbner ("Virch. Arch.," vol. lxxxviii.) found the bacilli in the blood. His attempts to transmit the disease to monkeys did not succeed. He is thus inclined to question Neisser's demonstration of its transmissibility.

In *Lepra anæsthetica* the skin is usually smooth and shining. This form has therefore been distinguished as *L. lævis* or *glabra*. White or brown stains appear on the skin at times, probably at the site of a former infiltration. This variety is described as *Lepra maculosa*; the patches as *morphœæ nigræ* or *albæ* (not to be confounded with the skin disease Morphœa).]

Lupus.

132. **Lupus** (or "*noli me tangere*") is an affection of the skin and contiguous mucous membranes. The surface becomes red, and this is fol-

FIG. 37.—Section of Skin through a Lupus-patch. *a*, normal epidermis; *b*, normal corium with sweat gland (*i*); *c*, focus of lupus-tissue; *d*, vascular nodule surrounded by diffuse cellular infiltration; *e*, non-vascular nodule; *f*, strings of cells; *g*, lupous ulcer; *h*, proliferating epithelium.

lowed by the formation of large or small nodules (Fig. 37, *d*) with more diffused swellings. Granulation-tissue is formed in the corium and subcutaneous connective tissue.

The granulations are generally vascular, the cells small, spherical, and

lymphoid; but at times numerous epithelioid cells and giant-cells may also be found. In the latter case, nodules may also develop having the exact appearance of tubercles. Surrounding the true granulomatous focus there are found nests and strings of cells following the course of the lymphatics (Fig. 37, *e*, *f*). When the subepithelial granulations have reached a certain degree of development, they begin to break down and ulcerate (Fig. 37, *g*). It seldom happens that ulceration is averted by reabsorption or cicatrization.

The exciting cause of lupus is unknown. The general course of the process, and especially its progressive character, seem to indicate that it is due to some virus capable of reproduction.

[Schüller ("Centralb. f. Chir.," 49, 1881) has found certain micrococci in lupus-tissue, which he holds to be the cause of the affection. His observations are not, however, enough to establish the fact with certainty.]

Glanders.

133. **Glanders** (or *Equinia*) is a contagious disease of the horse, communicable to man by direct transmission. Glanders and **farcy** are manifestations of one and the same infective disease; the first affects chiefly the nasal mucous membranes, the second the skin.

The initial lesion in the horse is usually situated in the nasal mucous membrane. The submaxillary gland is then affected; and then, by metastasis, various other organs. The first effect of the infection is to give rise either to wide-spread cellular infiltration of the mucous membrane, or to subepithelial nodules from the size of a millet-seed to that of a pea, and not unlike those of lupus. In chronic farcy larger nodes and nodules form in the skin, and sometimes link themselves into vermiform cords ("corded veins").

The epithelial nodules are very unstable in structure. The cellular elements of which they are built up maintain throughout the characters of lymphoid cells or pus-corpuscles. Owing to fatty change, disintegration, softening, or suppuration in the nodules, ulcerations are soon formed which have a yellowish infiltrated base. These grow by progressive nodular (or simply diffused) infiltration of their borders, followed by gradual disintegration. In this way contiguous ulcers may become confluent. In horses that have died of glanders, the mucous membrane of the nasal septum is beset with large irregular excavated ulcers with eroded edges and grayish or yellowish bases. In addition to these, there are other minute lenticular ulcerations, and gray or yellow nodular patches on the point of breaking down. The whole process is near akin to that of suppurative inflammation. The ulcers may heal up by the formation of irregular puckered cicatrices.

The cervical glands are always inflamed and swollen. Among the viscera the lungs are the most liable to be affected. They contain either

nodes with caseous detritus in the centre and a grayish cellular periphery ; or on the other hand lobular pneumonic patches of a light gray or blood-stained color, or opaque and yellow from fatty and caseous change. At times the alimentary mucous membrane contains nodes of various sizes, composed either of light gray cellular tissue, or of opaque yellowish-white caseous or suppurative matters. In farcy, which is usually chronic, the nodes ("buttons" or "buds") formed in the skin and muscles are made up of small-celled granulation-tissue, which later on undergoes retrogressive change, and becomes caseous or breaks down.

In man, as in the horse, infection with glanders-poison is followed by the formation of nodes and nodules, especially in the nasal cavities and frontal sinuses, and in the larynx and trachea. At the same time vesicular and pustular eruptions appear on the skin, followed by phlegmonous abscesses in the skin and muscles. The viscera are also affected in like manner. The development of the granulation-tissue is generally very imperfect ; the inflammation tends rather to take on a suppurative character. In chronic farcy large nodes ("farcy buds") are formed in the skin and muscles. When these break down they give rise to indolent and obstinate ulcerations.

[For a fuller description of equine glanders and farcy see Youatt, "On the Horse," London, 1859 ; Fleming, "Man. of Veterin. Sanitary Science," vol. i., London, 1875 ; on the human affection see Poland, "Holmes's System of Surgery," vol. i.

The nature of the glanders-poison is unknown. See Villemin ("Études sur la tuberculose," Paris, 1868), Bollinger ("Ziemssen's Cyclopædia," vol. iii.), and Pütz ("Die Seuchen und Herdekrankheiten," Stuttgart, 1882).]

Actinomycosis.

134. **Actinomycosis** is a progressive inflammatory affection, set up by a certain fungus, the *Actinomyces*. It results in the formation of granulations and fibrous tissue, and in suppuration. It attacks human beings, cattle, and swine, and may be communicated to cattle by inoculation.

The disorder was first recognized and described in man by Israel (1877), and in cattle by Bollinger (1877).

The parasite which causes the disorder is a peculiar fungus. It first appears as a tufted rosette of radiating pyriform or club-shaped structures ; these are either simple or divided by dissepiments, and are of considerable bulk. They are possibly the conidia (Art. 213). The fungus on reaching its full development appears as a peculiar gland-like body, with the outward form of a mulberry. It is produced by the aggregation of the club-shaped conidia ; these spring in all directions from the filaments of a matted tuft which we may provisionally call the mycelium,

and are thus crowded into a compact mass. The true botanical position of the fungus is as yet undetermined.

When the actinomyces settles in a tissue, it at once sets up inflammation in its neighborhood. While the spore is devéloping its mycelium and its bunch ("gland" or "core") of conidia, a nodular inflammatory focus is formed around it, which in its structure exactly resembles a tuberculous nodule. Recent nodules consist chiefly of round-cells; in less recent ones the zone in contact with the fungus-core contains epithelioid cells and giant-cells. The core is yellowish in tint, and in later stages of the process it often becomes calcified.

When the nodules increase greatly in number and become confluent, the internodular inflammation also extending, large areas of inflammatory swelling are formed. In many cases, and especially in cattle, scar-like bands of fibrous tissue may be formed in the spaces between the nodules. The nodules themselves usually break down and suppurate. If the tendency to further development be strong enough, we may have, instead of suppuration, large nodular patches of new tissue formed. These may grow for weeks or months and finally become as large as the fist, or larger. The tumor is made up partly of coarse fibrous tissue, partly of granulations, with the intermediate stages. It always contains small pus-cavities and other excavations, in which the fungus-cores are found as small white or yellow greasy-like masses lying among the purulent detritus.

If on the other hand the tendency to disintegration and suppuration prove the stronger, we have formed large sacculated cavities with branching intercommunicating fistulæ. The walls of these are lined with granulations and hyperplastic fibrous tissue, containing here and there colonies of the fungus.

135. In the case of cattle the disorder attacks chiefly the lower jaw; then the upper jaw, tongue, pharynx, larynx, œsophagus, stomach, and intestinal wall. The skin, the lungs, and the subcutaneous and intermuscular connective tissue are also liable to invasion. In these sites it generally gives rise to nodular tumors of various sizes, such as we have described. Till the true nature of the disease was made out, these were described by a multitude of names, such as osteo-sarcoma, bone-canker, bone-tubercle, fibro-plastic degeneration, woody-tongue, lingual tuberculosis, lymphoma, fibroma, spina ventosa, etc. In the cases observed in the human subject the disease has chiefly attacked the soft parts of the neck, the thorax near the spine, the mediastinal tissue, and the lungs. In one case the infective matter had entered the blood, and gave rise to metastatic foci in the viscera (Ponfick).

The inflammatory growths seldom reach any great size in man; they are apt rather to break down early. In the cases referred to, cavities and fistulæ were formed, some of them subcutaneous and some extending deeper. Among their purulent contents were found the fungus-cores. Where the process invaded the bone, it led to destructive caries; this

was notably the case with regard to the vertebræ. In all the affected regions the destruction of tissue was very considerable.

As regards the genesis of the disease, it seems very probable that the mouth is the starting-point of the infection. Israel, Johne, and Ponfick affirm that in healthy individuals the specific fungus is now and then found lying in the follicular crypts of the tonsils. It has also been discovered in concretions from the lacrimal duct, and in hollow teeth. The observations of the above authors, with those of Bollinger, make it probable that infection often follows upon wounds of the oral cavity (*e.g.*, those left after the extraction of teeth). Israel believes that the spores or fungi may be inhaled, and so give rise to the disease in the lungs.

Clinically speaking, the disease is chiefly marked by its chronic course and local malignancy. Metastasis is not common.

[Israel's researches were published in "Virch. Arch.," vols. lxxvi., lxxviii.; Bollinger's in the "Centralb. f. med. Wiss.," 27, 1877. Since then the affection has more than once been observed in man. Johne and Ponfick have been the chief writers on the human affection. Johne demonstrated the inoculability of the disease in animals ("Deutsch. Zeitsch. f. Thiermed.," vii., 1881). Ponfick has quite recently published a monograph ("Die Actinomycose des Menschen," Berlin, 1882), in which the published observations on the disease are brought together; light is thrown on its etiology by new observations and experiments; and the significance of the various morbid processes is explained. Gannet gives a useful summary in *Boston Med. and Surg. Journal*, August 31, 1882.

Pflug lately described a case of actinomycosis in a cow, which took the form of miliary nodules disseminated through the lungs ("Cent. f. med. Wiss.," 14, 1882); Hink (*ibid.*, 46, 1882) gives another case, in which the nodular affection was confined to a part of one lung.]

SECTION VI.

TUMORS.

CHAPTER XXV.

GENERAL CONSIDERATIONS.

136. In Arts. 79–92, under the heading of Hyperplasia and Regeneration, we discussed a series of progressive or formative disturbances of nutrition. Some of these were the result of normal development carried to an excessive degree. Others seemed due to the resumption or intensification of processes of growth which had been interrupted or enfeebled. These processes led to the formation of new tissue, which either resembled exactly the matrix-tissue from which it arose, or at least was composed of the same elements.

Another mode of tissue-formation was discussed in the last section, under Inflammation. This process, as we saw, gave rise only to a single form of new tissue; it resulted in the development of granulations and fibrous tissue from them.

The mode of tissue-formation which leads to the development of a **tumor,** neoplasm, or new growth in the restricted sense of the term, is not comparable either with hyperplastic proliferation or with inflammation. It differs from the former in this, that the new tissue is not similar to the matrix-tissue, but specifically different from it. A true tumor or neoplasm proper is always composed of tissue differing in type from that out of which it grows. It is distinguished from inflammatory tissue by the great variety of forms it may assume, and by the mode of its genesis.

The diversity existing between the neoplasm and the matrix is manifested in two ways. First, the new-formed tissue appears as a more or less sharply bounded and defined mass. Secondly, its texture and structure differ from those of its matrix, and generally to such an extent that the difference is recognizable with the unaided eye; it is of course still more plainly marked under the microscope. These two marks are generally enough to determine the diagnosis of tumor, though not invariably. In a whole series of new-formations, it is difficult or even impossible to distinguish anatomically between hyperplastic or inflammatory tissue and true neoplasm. The distinction must in such cases be based on the life-history of the tissue in question.

It should be noted—by way of distinction between inflammatory tissue and a neoplasm—that the latter does not originate in extravasated

blood-cells, so far at least as its essential elements are concerned. As distinguished from hyperplasia, the genesis of a neoplasm is not dependent on exaggerated function or increased activity in the affected organ; moreover it does not retrogress, but continues to grow on without reaching any particular or typical termination.

[The term tumor, or neoplasm, has been very differently interpreted by different writers. Virchow, for example, includes all hyperplasias and inflammatory or granulomatous formations among the tumors; while Cohnheim definitely excludes them. Others take up a middle position. This difference of view is closely connected with the different theories held concerning the etiology of tumors (Arts. 177–181). We think with Cohnheim that it is better to narrow the meaning of the term tumor so as to exclude hyperplasias and the infective granulomatous growths.

References: Virchow ("Die krankhaften Geschwülste"); Lücke ("Handb. d. Chir. v. Pitha u. Billroth," vol. ii.); R. Meier ("Lehrb. d. allg. Path.," 1871); Cohnheim ("Allg. Path."); Paget ("Surgical Path.").]

137. Tumors have been distinguished by various names according to their external form. **Nodular** tumors are made up of circumscribed nodes or nodules, single or grouped. Nodules of the size of a millet-seed are called miliary; smaller ones submiliary. If the neoplasm is imperfectly marked off from its matrix, and extends into it by continuous or disconnected outgrowths, it is called **infiltrating**. The terms nodular and infiltrating are not, however, antithetical. A tumor may have nodes and nodules, and yet infiltrate the tissue in which it lies. This latter depends on the mode of growth. If the tumor increase interstitially ("central" or "expansive" growth), it merely compresses and thrusts away the surrounding tissue, but does not infiltrate it. If it grows at the periphery by including ever fresh portions of the matrix-tissue ("appositional" or "eccentric" growth), it will give rise to the appearance of infiltration.

A tumor seated on any of the surfaces of the body, and protruding so as to form a segment of a spheroid, is said to be **tuberous**. If the base be smaller than the body of the tumor, it is **fungous**. If stalked, it is **polypous** or pedunculated. If it consist of several small and close-set protuberances, like the papillæ of the skin, rising from a common stalk or base, the tumor is called warty, verrucose, papillomatous, or briefly a **papilloma**. If the papillæ are very long and branched, it is described as a dendritic or ramifying growth.

138. The texture and structure of tumors are very various. A large group consists of tissues resembling some of the adult or embryonic connective tissues; they are thus made up solely of mesoblastic elements. Such are distinguished as **histioid** tumors, or more simply as **connec-**

tive-tissue tumors. Some of them are firm and of the texture of fibrous tissue, cartilage, or bone. Others are soft and contain adipose tissue, mucous tissue, or embryonic or indifferent tissue. Very soft varieties, resembling brain on section and yielding a white creamy juice on being scraped, are described as encephaloid or medullary. Not uncommonly a tumor may have a different texture in different parts of it; it is then spoken of as a mixed tumor. It arises when two distinct tissue-forms are simultaneously developed, or when a single tissue has undergone partial transformation into another.

A second group of tumors are more complex in structure. They consist not only of mesoblastic elements, but of epiblastic and hypoblastic elements in addition; in other words they contain elements derived from epithelial cells. They are therefore described as **epithelial** tumors, in contradistinction to the connective-tissue group. Inasmuch as they exhibit a certain similarity of structure with various organs of the body, they have also been called **organoid** tumors. Their structure may often be recognized with the naked eye. On section the general appearance is that of a dense basis-substance, built up of reticulated bands and trabeculæ, and containing within its meshes a substance of different color and softer consistence. The latter often takes the form of a milky or creamy juice. Medullary forms are also met with in this group.

[A tumor resembling its matrix-tissue in texture Virchow calls **homœoplastic**; one which differs widely is **heteroplastic**. The latter term implies that in normal circumstances tissue like that of the tumor never occurs at all at the spot in question; or at any rate not at the particular stage of development reached at the time in question. A tumor may thus be heteroplastic as regards its site (heterotopic), or as regards its date (heterochronic). By excluding the mere hyperplasias from the category of tumors, we are bound in strictness to regard all tumors as heteroplastic; they never are of exactly the same structure as the matrix-tissue. A division of tumors into homologous and heterologous growths has been proposed. Homologous growths are such as resemble some normal tissue of the body; heterologous growths such as resemble no mature normal tissue. Unless a homologous growth is heterotopic it is not distinguishable from a hyperplasia. A growth which is strictly heterologous must be heteroplastic.]

139. Every tumor is developed from pre-existing tissue-cells by proliferation; in some tumors new blood-vessels are also formed. The processes of cell-division and of vascularization are identical with those described in Arts. 74 and 86. Nuclear subdivision is indirect; new vessels are formed by off-shoots from existing ones.

Tumors usually develop from small beginnings. It is rarely that their site of origin extends over an entire organ. From this it follows that they do not usually lead to an enlargement of the organ as a whole, but

rather tend to form definite nodes or protuberances. Some grow with great rapidity ; others slowly and intermittently. There is no limit to their growth ; they often reach enormous dimensions. They may cease to grow at all for years together, and then suddenly begin again.

Neoplastic or tumor-tissue is very liable to retrogressive changes ; this is especially true of quickly growing cellular tumors. All the retrogressive changes which affect normal tissues are observed in tumors—fatty degeneration, mucoid degeneration, necrosis, caseation, disintegration, softening, liquefaction, gangrene, infarction, calcification, pigmentation (as in melanoma), etc. Inflammations are also very common in tumors.

Any of these processes may lead to partial destruction of a tumor. Cavities or ulcers are often formed in consequence of softening, and the new tissue may thus be disintegrated and destroyed—slowly or rapidly as the case may be. It is unfortunate that this process does not usually bring about the removal and eradication of the tumor, especially in the so-called malignant forms. The centre may break down, but the periphery continues steadily to advance. It may even happen that the peripheral advance is accelerated by the inflammatory disintegration of the central parts.

[It is highly probable that, during the development of a neoplasm, the walls of the blood-vessels are somehow damaged or impaired. In support of this it may be mentioned that in the neighborhood of tumors we always find aggregations of small extravasated leucocytes. The manner in which this impairment of the vessel-walls is brought about remains unknown.]

140. Most tumors are solitary. In other words, there is originally but a single primary tumor. It is less frequent to find two tumors growing in an organ simultaneously, or in quick succession. In the latter case we must suppose that appropriate conditions arise at the same time at the different sites. Now and again it happens that several tumors, all of different structure, appear simultaneously in the same person.

From such multiple primary neoplasms we must of course distinguish what are called metastatic formations. **Metastasis** in this case implies a secondary neoplastic eruption, resulting from the transmission of elements of the original or parent tumor to a remote part of the body, and the development of a daughter-tumor from these germinal elements.

The germ or other virus given off by the parent tumor is conveyed to other regions through the lymphatics, or through the blood-vessels. According to the channel of transport, we find metastatic affections in the lymphatic vessels and glands which receive the infected lymph ; or in remote organs irrigated by the infected blood, either directly or after passing through the heart. Thus in cancerous disease of the intestine we find secondary nodules developed in the liver, through the medium of

the portal system; from the liver some germs may even find their way into the lungs. The germinal elements usually reach the blood by the direct penetration of the tumor-tissue into the lumen of a blood-vessel.

The development of the daughter-tumor starts unquestionably from these transported germs. This is probable *à priori* from the fact that the metastatic or secondary tumor has always the same structure as the primary. The germs are, furthermore, essentially composed of cells in a condition of vital activity. The share taken by the matrix-tissue in which the germs are deposited is not always the same. In all cases it must furnish the necessary nutriment and blood-vessels, for without these no new growth is possible. But it very often furnishes other elements, and especially connective tissue. Proliferation is set up around the transplanted germs, and tissue is thereby formed; while migratory leucocytes generally contribute something to the whole. The secondary tumors developed may vary greatly in number. They are usually marked off definitely from the surrounding tissue; it is very uncommon for metastases of the kind to take the form of diffuse infiltration. This happens (if at all) in the case of bone, which may be transformed into tumor-tissue by secondary change affecting almost the entire skeleton.

Metastases are not invariably produced by all tumors; many of these never extend beyond the limits of their primary seat. The clinical character of **benignancy** or innocency is generally correlated with this property of tumors; **malignancy** is a character of the metastatic varieties. Other marks of malignancy are the tendency to infiltrate and so destroy the surrounding tissue, and the tendency to recur after apparent extirpation.

[Malignancy, or the tendency of a tumor to invade the neighboring tissue and to produce metastatic tumors, is usually regarded as an inherent property of the tumor. Cohnheim has recently expressed a different opinion ("Allg. Path.," i.). He tries to explain malignancy by assuming that the physiological resistances to invasion are somehow diminished. Germs transplanted into fresh tissue are sure, he thinks, to perish in consequence of the normal chemical or metabolic changes which go on in the tissue. They can only develop when these metabolic changes cease to be normal. His main ground for this view is derived from an experiment made by himself and Maas ("Virch. Arch.," vol. lxx.). They introduced pieces of living periosteum into the pulmonary vessels, and found that they grew for a time, but were ultimately absorbed and disappeared. The diminished resisting power of the tissues may be either congenital or acquired. The latter is especially the case in advanced age.

Ziegler is unable fully to agree with this view. Though the condition of the tissue has undoubtedly a great influence on the development of a germ transplanted into it, yet this alone cannot determine the malignity

of the parent tumor. It surely depends on the structure and texture of the tumor whether its germs can be carried off at all and transported by the stream of lymph or blood. And the faculty of developing in proper circumstances must be inherent in the germs themselves. Zahn ("Sur le sort des tissus emplantés dans l'organisme," Geneva, 1878) found that fœtal tissues continued to grow for a time when introduced into the body of an animal. Leopold has quite recently confirmed this observation ("Virch. Arch.," vol. lxxxv.). Pieces of living tissue, taken from embryo rabbits and transplanted into other rabbits, are in part absorbed, and in part continue to grow. The latter is especially true of embryonic cartilage.]

141. The formation of a tumor is always more or less fraught with injury to the affected organ, and in many cases to the entire system. The least harmful tumors are those which grow slowly and by expansion, so that they merely compress the surrounding tissue. If this is expansible or yielding, like the skin, the resulting changes may be trifling. But it is not rare for the compressed tissue to become atrophied or absorbed. If the neoplasm be an infiltrating one, the surrounding tissue suffers much more seriously. It either perishes outright, or begins to proliferate and so contributes materials to the general growth. This is especially the fate of tissues which have specific functions; the specific elements die, while the fibrous or connective framework persists and becomes hyperplastic.

A tumor requires to be fed if it is to grow; hence the organ in which it is placed and the system generally are deprived of a certain proportion of nutriment to supply the tumor. If growth is slow the deprivation is unimportant, but it may become grave in the case of rapidly increasing tumors.

The seat of the tumor is of serious import. It need hardly be said, for instance, that a tumor growing in the brain or spinal cord has an altogether different significance, so far as life is concerned, from that of one developed in the skin. So also a tumor in the œsophagus obstructing the passage of food, or one in the stomach interfering with digestion, will lead to more serious results than one, say, in the bone of the finger. In the one case the function of an essential organ is impaired by the presence of the tumor, in the other the effects are merely local.

Metastatic or secondary formations have always an unfavorable significance. As the neoplastic foci become more numerous, so also do the organs exposed to the risk of injury by pressure, invasion, or abstraction of nutriment.

Disintegrative changes and ulcerations connected with tumors are specially destructive. There is nearly always an active secretion and loss of substance from the surface of such ulcers, and the body is reduced by the constant drain. Moreover, it is not uncommon for putrefactive changes to be set up in the products of disintegration, and then

the risk of blood-poisoning by absorption of septic matters becomes considerable.

Tumors may thus impair the function of essential organs, or give rise to a serious drain of matter from the body, or bring about a kind of blood-poisoning through the absorption of deleterious products of decay; in any or all of these ways the general nutrition may be profoundly disturbed, and the patient fall into grave ill-health. This is spoken of as the **cachexia** of tumor. It may become so profound that the patient dies of exhaustion.

CHAPTER XXVI.

TUMORS DEVELOPED IN MESOBLASTIC TISSUES—CONNECTIVE-TISSUE TUMORS.

a. Fibroma.

142. A **fibroma** is a tumor made up of fibrous tissue. It usually takes the form of a sharply defined node or lump, and occupies a part only of the organ in which it is seated. More rarely the organ (as *e.g.*, the ovary) becomes transformed throughout into a fibrous mass. Fibromata occurring on epithelial or mucous surfaces often take a papillomatous form.

The fibroma is of very varying consistence, according to the texture of its component tissue. It is often very firm and tough, grating under the knife, and having a glistening gristly look on section (desmoid fibroma). In other instances it may be soft and flabby, with a grayish translucent section. Other specimens will be found in which the scattered fibrous bands are dense and white and glistening, but the general structure is loose and incompact; so that the tumor, as a whole, is rendered limp and flabby. All varieties of intermediate forms occur between the firm and the soft, and even within the same tumor different parts may be of different consistence. The firm varieties are seen under the microscope to be made up chiefly of large coarse fibrous bundles, interspersed more or less thickly with cells whose protoplasm is scanty.

The softer fibromata, with their translucent grayish section, are usually richer in cells. By teasing out a fragment it is easy to isolate numbers of slender spindle-shaped or caudate cells. The intervening substance is more scanty, the fibrils less coarse and gathered into smaller bundles. Stained sections of such fibromata appear as if they were full of nuclei (Fig. 38).

In loose-textured fibromata a clear juice is contained between the fibrous bundles, which are crossed and plaited and interwoven in all directions.

The fibroma is developed from proliferous connective-tissue cells. Accordingly spots are often to be found in it where cells are more abundant than in the tumor generally; in such spots we find not only the slender spindle-shaped kind, but also round and oval cells, and even stellate cells. The transformation of the proliferated cellular tissue into

fibrous tissue is effected by the same steps as in fibrous hyperplasia (Art. 85).

Fibromata may occur in very various tissues ; in any structure indeed which contains any form of connective tissue. Thus they are found in the skin, nerves, ovary, periosteum, fasciæ, uterus, and less often in the mamma, alimentary canal, etc. Their appearance is always manifestly different from that of the matrix in which they are seated (Fig. 38). Fibromata do not give rise to metastatic or secondary tumors, though they are often enough multiple, especially in the skin, nerves, and uterus. Within the same tumor we may often make out several centres of growth ; the fibroma is, in fact, composed of several nodes separated by ordinary fibrous tissue. Such tumors can only do injury in virtue of their size or of their site.

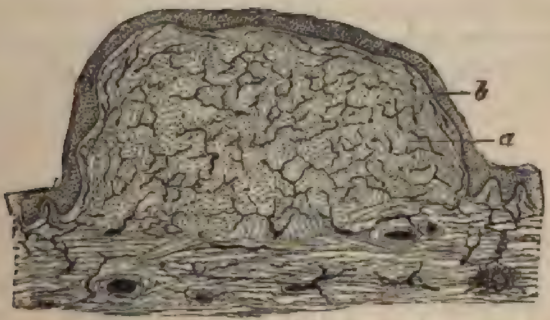

FIG. 38.—Fibroma Molluscum of the Skin. × 25. (Injected preparation stained with hæmatoxylin.) a, fibroma ; b, papilla thinned out by distention.

Now and then fibromata undergo degenerative changes. They may become fatty, or may soften and break down, so that cavities form within them. They may give way at the surface, and so ulcerate ; sometimes they become partially calcified, as in the case of uterine "fibroids." They may be highly vascular, or the reverse (Fig. 38). In rare cases the blood-vessels become wide and dilated, so that the tissue is pierced with capacious channels and cavities containing blood. In other instances the lymphatics are similarly dilated.

[It is not always easy to distinguish between true fibroma and fibrous hyperplasia. In general the fibroma is characterized by the difference between its texture and that of the surrounding tissue, from which, moreover, it is for the most part sharply defined. These characters are usually wanting in hyperplasias, such, for instance, as those consequent on chronic inflammation. Now and then, however, we meet with inflammatory hyperplasias which are circumscribed—such as venereal warts in the skin, and the nodes developed in the lungs around inhaled dust-particles. As in the last instance, their texture may be different from that of the matrix. It is the life-history and mode of genesis to which we must appeal

in such cases. Inflammatory hyperplasias, being mere products of inflammation, cannot properly be reckoned among the true tumors.]

b. *Myxoma.*

143. When the ground-substance of a fibroma swells up by the imbibition of fluid, it becomes gradually more and more translucent and may even become transparent. The tumor at length resembles a mass of jelly. A swollen fibrous tumor of this kind is best described as an œdematous fibroma. The texture of many œdematous fibromata much resembles that of the umbilical cord in nearly mature fœtuses; where the cells and fibrils are more or less thrust asunder and interpenetrated by a transparent juice (Wharton's jelly).

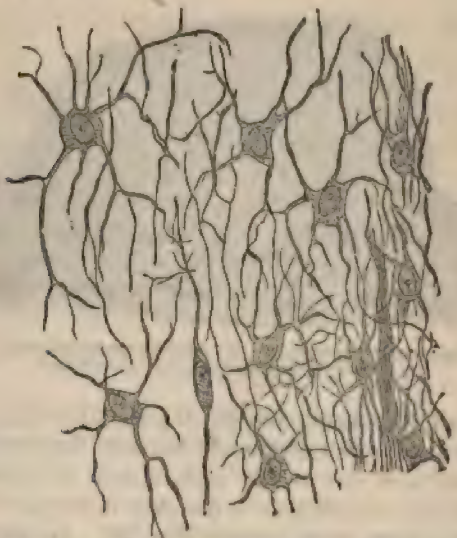

FIG. 39.—Cells from a Periosteal Myxoma of the Thigh. × 400. (Gold staining.)

Adipose tissue, whether neoplastic (Art. 144) or normal, may similarly become transformed into a gelatinous mass. The fat disappears from the cells, and a dense saline liquid collects between them. They ultimately assume a ramified or stellate form.

No sharp line can be drawn between jelly-like œdematous fibromata and lipomata, and true **myxoma.** Many writers do not hesitate to include the former class among the myxomata. It is perhaps more correct to reserve the name for tumors in which we have not only a swollen and semi-liquid condition of the interfibrillar substance (a substance normally containing mucin), but also an actual solution of the fibrillæ and replacement of them by dense saline juice. Such a tissue is highly translucent, almost transparent, in fact. The cells it contains are generally much ramified, though some remain rounded (Fig. 39). They here and there

undergo mucoid degeneration and so perish. Pure mucous tissue, such as we have just described, is never uniformly present throughout the tumor; there is no such thing as a perfectly pure myxoma. The bulk of the tumor is generally made up of œdematous connective tissue; some parts of it may even be coarsely fibrous. It is thus best described as **myxofibroma** or **myxolipoma,** as the case may be.

Myxomata are most commonly found in the fibrous tissue of the periosteum, skin, fasciæ, and muscular septa, as also in the subcutaneous and subserous fat, and in the marrow of bone. They are innocent and rarely give rise to metastases. On the other hand, they may grow to an inordinate size, and may also be multiple.

[Köster ("Sitzungsb. d. niederrhein. Ges. f. Natur- und Heilk.," January 17, 1881) and his pupil Rumler ("In. Diss. Bonn") have investigated the relation between myxoma and œdematous fibroma. Köster regards swollen and saturated connective tissue as identical with mucous tissue. Myxomata arise merely from the swelling up (by imbibition) of the ground-substance of the various connective tissues.]

c. Lipoma.

144. **Lipomata** are tumors composed of adipose tissue. They form soft or firm lobular masses, often of considerable size. Their structure is very much like that of the subcutaneous *panniculus adiposus;* it is made up of a series of fatty lobules bound together by fibrous septa of varying thickness. The lobules of the tumor are, however, rather larger than the normal ones.

If, as is not uncommon, we have mucous tissue associated with the adipose, the tumor is described as a **lipomyxoma;** if it contains abundant fibrous tissue it is a **lipofibroma.**

Lipomata generally arise from normal adipose tissue, though they may also be developed in connective tissues which normally contain no fat, such as the submucous coat of the intestine, and the dura mater. The larger lipomata not infrequently undergo either calcification, necrosis, gangrene, or putrid decomposition. They do not form metastases, though they are often multiple. The fat they contain is never completely absorbed, even when the patient becomes utterly emaciated.

d. Glioma.

145. **Gliomata** are tumors which develop from the neuroglia-cells of the central nervous system, and when mature are largely made up of neuroglia-cells. They are formed in the brain, and more rarely in the spinal cord. They appear as tumors which are imperfectly marked off from the healthy brain- or cord-substance; the margin of the tumor gradually merges into the healthy tissue. They have thus the look rather of

localized swellings than of tumors; but the difference in tint, and the blurring of the normal distinctions between the various elements of the brain-substance, serve to make good the diagnosis.

Their appearance varies. Some are light gray and translucent like the cortical substance, and fairly firm in consistence. Others are whiter, coarser, and firmer. Others again are grayish red or even dark red, in which case they are traversed by large and numerous blood-vessels. Vascular gliomata often enclose hemorrhagic patches. They are subject to fatty degeneration, caseation, softening, and disintegration.

A section of a mature glioma exhibits under the microscope a kind of felted texture, made up of excessively fine lustrous filaments (Fig. 40, *B*) interspersed with a multitude of slightly oval nuclei. The nuclei are surrounded by a scanty hardly visible protoplasm. If, however, the prep-

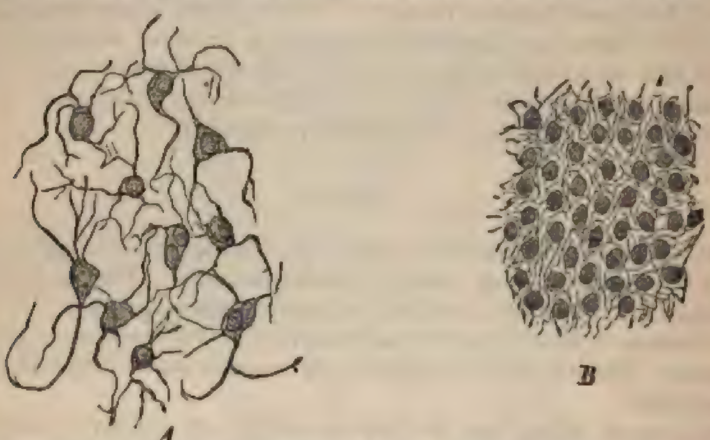

FIG. 40.—Glioma from the Brain. × 350. *A*, cells isolated by teasing and stained with carmine. *B*, section of the same tumor hardened in Müller's fluid, mounted in Canada balsam, and stained with aniline brown.

aration be examined when quite fresh, or after treatment with Müller's fluid, it is readily seen that the nuclei belong to cells which are furnished with numerous delicate ramifying processes going off in various directions (Fig. 40, *A*). These cells are very similar to neuroglia-cells, though they are often decidedly larger and coarser. Some of them may contain two, three, or more nuclei.

Researches on the development of glioma have shown that the neuroglia-cells are the parent cells to the tumor. The ganglion-cells take no part in the proliferous process. The proportion of cells in the tumor varies greatly; sometimes the cells form the bulk of it, and sometimes the fibrous framework.

The vessels are often highly developed, and may be sacculated or generally dilated.

Glioma is usually solitary, and as regards metastasis is innocent; it is only locally malignant.

Certain cellular tumors of the retina have been described as gliomatous; their elements resemble the cells of the granular layer. As they grow they invade on the one hand the orbital cavity behind the eyeball, or on the other hand break through the cornea and sclerotic, passing forward. They recur after apparent extirpation, and give rise to metastases. The cells in which they are made up are partly round and simple, and partly ramified. It seems questionable whether we are justified in calling these tumors gliomata. We are inclined to maintain that they are really sarcomata.

[Glioma was first defined and named by Virchow ("Die k. Geschwülste," ii., ch. 18). Klebs has recently propounded the theory ("Beiträge zur Geschwulstehre," i., 1879) that the ganglion-cells play an active part in the formation of gliomata. Ziegler and Christoph examined a large number of gliomata, both fresh and hardened, but failed altogether to find evidence for this view. The nuclei of the ganglion-cells seemed never to subdivide. In the instances where this at first sight appeared to occur, closer investigation showed that the suspected ganglion-cell had merely incorporated a neuroglia-cell.]

e. *Chondroma.*

146. **Chondromata** (or enchondromata) are tumors which consist essentially of cartilage. The slight amount of fibrous tissue usually present in a chondroma is of altogether minor importance. It either serves to cover the surface of the tumor, or penetrates the interior, carrying the nutrient blood-vessels.

Cartilaginous tumors are chiefly developed in regions which normally contain cartilage; that is to say, in the osseous system or in the cartilaginous parts of the respiratory system. They may occur, however, in tissues which are normally devoid of cartilage, such as the testis and parotid gland, and more rarely in other organs. They are of very various size; the smaller ones are generally globular, the larger are lobed or nodular. The several lobes are in the latter case separated by fibrous tissue. They are often multiple, especially in the skeletal structures of the hands and feet.

The tumor-tissue has usually the structure of hyaline cartilage, though sometimes yellow cartilage or fibro-cartilage largely replaces it. Even in hyaline chondromata, however, there are always patches in which the matrix-substance is beset with fibres. At the periphery the cartilage passes gradually into fibrous tissue, which forms a sort of perichondrium. The hyaline matrix often has a dusty or ground-glass appearance.

The number, size, shape, and grouping of the cartilage-cells vary much in different cases, and even within the same tumor. Many tumors abound in cells, in others they are sparse; in some the cells are large, in others small. They may be surrounded by capsules, or they may be

naked ; and crowded in groups within single capsules, or more uniformly scattered. Every variety of normal cartilage may occur also in chondromata. The form of the cells varies accordingly ; they are usually spherical, but fusiform and stellate cells are not uncommon, especially in the neighborhood of the fibrous septa which divide or surround the lobules of the tumor. So far as the development of the tissue is concerned, all that was said in Art. 87 applies also here. The matrix is derived either from pre-existing cartilage, or from marrow, periosteum, bone, or other connective tissue. Cartilaginous tumors which originate in cartilage have been called **ecchondroses** (*cf.* exostoses).

Chondromatous tissue is very apt to undergo retrogressive change. Some of the cells generally contain oil-globules. In large tumors the matrix-substance frequently undergoes mucoid softening and liquefaction, at points scattered here and there through it. This results in the formation of mucous tissue (Arts. 90–92) ; or in complete liquefaction of the matrix and destruction of the cells, and so in the formation of cysts containing liquid. In other cases the cartilage becomes calcified, or true bone is developed (Art. 165). Sarcomatous tissue may be produced when the cartilage-cells multiply rapidly.

Chondromata are generally speaking innocent, though metastases are occasionally met with.

[In reference to cartilaginous growths, we must be careful to distinguish hyperplasia from true neoplasm. We must not set down all cartilaginous formations as chondromata, even when they are extensive. We often find considerable cartilaginous growths in connection with bones (especially at the articular ends), which are quite certainly to be regarded as hyperplastic. It is the general course of the process which must decide in each case. The more completely a growth differs from its matrix, and develops as an independent tissue, the more certain we are that it is a real tumor.

Virchow ("Monatsber. d. Acad. d. Wiss.," Berlin, 1875) has made it probable that many osseous enchondromata originate in remnants of cartilage which have abnormally remained unossified. Such quiescent islands of cartilage certainly exist and are not at all uncommon ; it may well happen that they suddenly resume the habit of growth and begin to proliferate. Virchow suggests (by way of accounting for parotid enchondromata) that outlying bits of fœtal cartilage may lodge in the rudimental parotid gland, which properly belong to the rudimental pinna of the ear. See Paget, "Surg. Path.," Lect. 26 ; "Medico-Chir. Trans.," 1855 ; Ranvier, "Bull. Soc. Anat.," 1865 ; Virchow and Hirsch, "Virch. Jahresber.," 1869.]

f. Osteoma.

147. The **osteomata** are tumors composed of osseous tissue. Their usual seat is in connection with the bones, though they may occur elsewhere.

Osseous formations connected with the bones have received different names according to their site and disposition. **Hyperostosis** is diffused and extensive overgrowth in a bone. When the new-formed tissue is seated upon a definite spot in the old bone it is described as an **osteophyte**; or, if it be larger and more like a tumor, as an **exostosis.** Circumscribed bony growths in the interior of bones are called **enostoses.** Bony growths which are not rigidly connected with the bone are divided into—mobile periosteal exostoses, which are seated on the periosteum though separate from the bone; parosteal osteomata placed near to the bone, but not connected with it; independent osteomata remote from the bone and seated in tendon or muscle; and finally, the strictly **heteroplastic osteomata,** which may be seated in the lungs, brain-membranes, diaphragm, skin (rarely), parotid gland, etc.

Excrescences also occur in connection with the teeth. If they consist of cement or *crusta petrosa*, they are called dental osteomata; if they consist of dentine they are odontomata. The latter originate in a hyperplasia of the pulp during the development of the tooth.

The texture of an osseous tumor may resemble that of ivory, as in eburnated osteoma; or it may be soft and spongy, as in spongy or cancellous osteoma; the former varieties are built up of dense and compact tissue with narrow nutrient canals, and similar to the cortical layer of the long bones. The latter are built of thin and delicate trabeculæ enclosing large medullary spaces; they are allied in texture to cancellous bone.

The surface is sometimes uniform and smooth, so that the entire tumor is conical, spherical, or pyriform; sometimes it is irregular, rough, or tuberculated, without any definite figure. Ivory-like tumors are generally of the first kind; they occur most commonly as exostoses of the skull. Spongy exostoses are of the second kind, as are also the independent and heteroplastic osteomata.

The development of the osseous tissue in tumors follows the course described in Art. 88. It is effected partly by the agency of osteoblasts, partly by metaplasia of the existing tissue. The ground-substance is chiefly derived from the connective tissue of the periosteum and of the structures in which the tumor is bedded; as well as from cartilage and bone-marrow. When cartilage is first produced by periosteal proliferation, and then transformed into bone, the growth is described as a cartilaginous exostosis. When bone is directly produced, by suppression of the cartilaginous stage, we have a fibrous exostosis.

Many abnormal bony growths are not, strictly speaking, tumors, but rather hyperplasias resulting from excessive growth or inflammation. This is true not only of most hyperostoses, osteophytes, and exostoses, but also of some parostoses and independent osteomata. Of this nature are the bony growths produced in the adductors of the thigh by constant riding, and in the deltoid by the shouldering of the rifle in manual-exercise. In what way fibrous tissues which never produce bone nor-

mally are excited to produce it by long-continued irritation, is not easy to determine. We only know that the occurrence is not by any means impossible. The diagnosis between true and false osteoma is not always easy. If the new growth is unaccompanied by signs of irritation or of inflammatory change in its neighborhood, it is probably a true osteoma.

[References :—Müller, "Zeitsch. f. wiss. Zool.," ix. ; Paget, "Surg. Path.," Lect. 27 ; Virchow, "Die k. Geschwülste."]

g. Angioma.

148. **Angiomata** are tumors principally made up of blood-vessels. Some of these blood-vessels may be new-formed, others are pre-existing vessels more or less altered. The alteration is chiefly in the direction of dilatation, or thickening of the walls. Angiomata are not sharply marked off from the surrounding tissue. According to our definition of tumor, which makes the formation of new tissue an essential feature, we should exclude from the angiomata all vascular tumors which are produced merely by the dilatation or overgrowth of pre-existing vessels.

General usage has, however, sanctioned a certain relaxation of this strict rule, inasmuch as simple vascular dilatations extending over a definite region, and so giving rise to a definite tumor-like swelling, are universally described as angiomata. According to its structure the angioma is spoken of as simple or cavernous. Racemose aneurisms, and racemose varices, have also been included among vascular tumors ; and a fifth variety is furnished by lymphatic angioma or lymphangioma.

149. **Simple angioma** (telangiectasis or simple erectile tumor) is a structure made up of some normal basis-tissue, containing an abnormal number of distended and altered veins and capillaries.

Such formations are most frequently met with in the skin ; they are usually congenital, and after birth merely increase in size. They are described as vascular **nævi**, and chiefly occur at places where fœtal clefts have become closed (fissural angiomata). They can hardly be spoken of as tumors, for they do not raise the skin. A simple nævus merely looks like a level patch of a different tissue substituted for the normal skin. The color is either bright red (*n. flammeus*, strawberry mark), or livid (*n. vinosus*, port-wine mark). It is not usually marked off very sharply from the normal tissue. Small circumscribed red specks are often found round the edges and in the neighborhood of the chief patch. The red color is due to the wide and distended blood-vessels, which are seated in the corium or subcutaneous fat. In the latter site they are often beset with minute sacculations. It is rare for such nævoid angiomata to be found elsewhere than in the skin ; but they occur now and then in glands like the mamma, in bone, and in the brain. They occur also, and more frequently, in the interior of morbid growths, such as gliomata and sarcomata.

When the vascular changes are more closely examined, by isolating the vessels or by making sections of the tumor, it is seen that they depend essentially on localized dilatations of new-formed or pre-existing capillaries (Fig. 41). The dilatations are fusiform, cylindrical, sacculated, or spherical; and these varieties of form are combined in all possible ways. In nævi the dilatations are even more exaggerated than those in the figure. They form wide cavities connected together by normal or but slightly dilated capillaries. The walls of the capillaries are not perceptibly thicker than the normal; they have thus the appearance of being rather thin than otherwise.

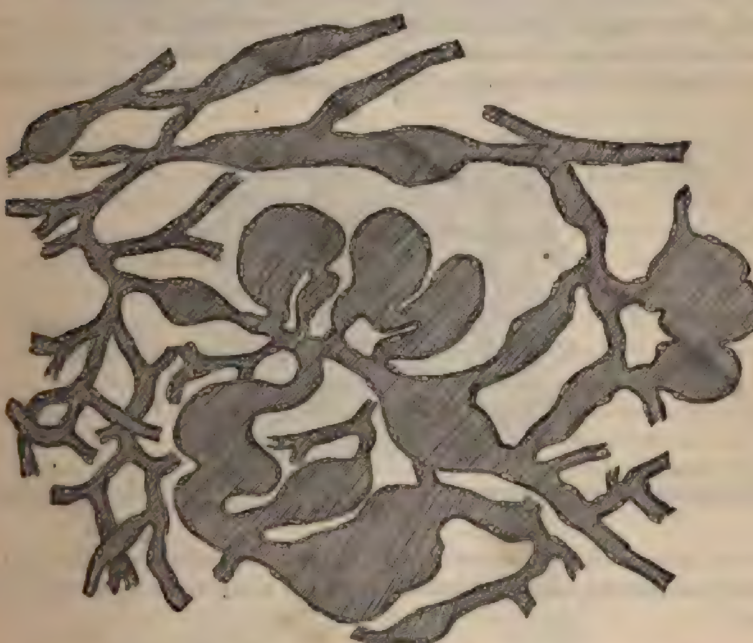

FIG. 41.—Dilated Capillaries from a Simple Angioma of the Brain. × 200. (Isolated by removal of the basis-tissue.)

Another form of simple angioma, best described as the hypertrophic form, is made up of dilated capillaries whose walls are very considerably thickened. The dilatations are not usually so extreme as in the former varieties, but the number of vessels is so vast that on section they seem everywhere contiguous, the basis-tissue being as it were thrust out of sight (Fig. 42). The capillary-walls are abnormally thickened and beset with nuclei, resembling somewhat the walls of the arterioles. When the blood is abstracted and the lumen of the vessels diminished as much as possible, so that the nuclei are set radially, the section looks very like one through the glomerulus of a sweat-gland. This resemblance is further increased by the fact that the tumor is made up of a number of lobules or nodules

separated by fibrous tissue, each composed of a convoluted knot of hypertrophied vessels. Moreover, as these angiomata occur in the skin, and chiefly in the deeper parts of the cutis and subcutaneous connective tissue, it sometimes happens that the section includes actual sudoriferous tubules (Fig. 42).

A third form of simple angioma is the venous or varicose tumor; it likewise occurs chiefly in the skin and subcutaneous tissues. In the forms already described the smaller veins are often dilated, but this feature is not marked in comparison with the capillary changes. In the venous angiomata the dilatation is almost entirely confined to the smaller veins, the anastomosing capillaries remaining almost unchanged. The venous dilatations or varices are cylindrical, ampullate, or saccular, with distinct and somewhat thickened walls. **Hæmorrhoids** or piles are of this nature; they are tumors formed in the mucous membrane of the rectum

Simple { Naevi
Hypertrophic
Varicose tumor

FIG. 42.—Section of a Simple Hypertrophic Angioma of the Skin. × 200. The duct of a sweat-gland has been cut across at the middle of the section.

near the anus, and consist mainly of hyperplastic submucous tissue, and of blood-containing saccules, derived from the small veins by morbid dilatation.

[References :—Rokitansky, "Lehrb. d. path. Anat.," 1855; Virchow, "Die krankhaften Geschwülste;" Billroth, "Arch. f. Chir.," xi.; Lücke, "Chirurgie v. Pitha u. Billroth," ii.; Monod, "Étude sur l'angiome simple," Paris, 1873; Paget, "Surg. Path.," Lecture 28 (containing further references).]

150. The **cavernous angioma** is distinguished from the simple angioma by the fact that the tubular form of the vessels is more or less lost. In its fully developed form, the tumor is made up of a series of wide variously shaped cavities, separated from each other merely by fibrous septa (Fig. 43). In section these cavities appear as sinuses of various size, separated by a trabecular network of nucleated fibrous or spindle-celled tissue. The separation is not complete, as the spaces com-

municate with each other. The mass resembles greatly the corpus cavernosum of the penis, and is sometimes described as composed of "erectile" tissue. The walls of the cavities are lined with endothelium.

These tumors are commonly seated in the skin, and may be congenital (Fig. 43). In other cases they are developed from simple angiomata by

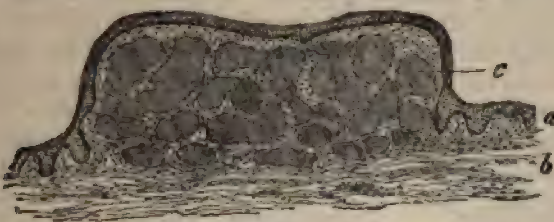

FIG. 43.—Congenital Cavernous Angioma of the Skin. × 20. (Hæmatoxylin staining.) *a*, epidermis; *b*, corium; *c*, cavernous blood-spaces.

continued dilatation of the already dilated vessels. In the skin they form livid, raised, and sometimes uneven patches (*nævus prominens*). Among the viscera the liver is by far the commonest seat. Here they take the form of dark brown patches, not raised above the surface, and not compressing the liver-tissue, which, indeed, they simply replace. They are never congenital, but are developed in advanced age when the liver is tending toward atrophy. It is easy to make out in favorable specimens that the cavities have arisen from the varicose dilatation of individual capillaries within the lobules, the liver-cells disappearing simultaneously (Fig. 44). At first there is no proliferation from the vessel-walls. Then several capillaries coalesce by disappearance of the septa, and so form larger cavities. When the cavernous metamorphosis reaches the border of a lobule, the periportal fibrous tissue forms a cap-

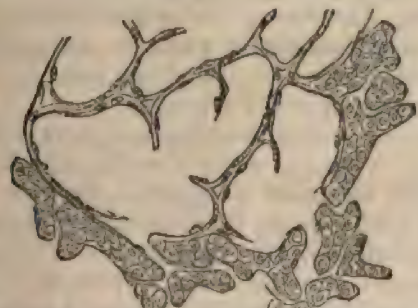

FIG. 44.—Section from the advancing Border of a very small Cavernous Angioma of the Liver. × 150.

sule round the transformed vascular mass, which at first has no definite boundary. At this stage proliferation of the tissue not infrequently sets in (*cf.* Rindfleisch, "Path. Hist.," vol. i., p. 163).

Angiomata are found, though very rarely, in the kidney, spleen, uterus, intestine, bladder, muscles, bones, etc.

[The above account of the development of cavernous tumors in the liver is considerably at variance with that given by Virchow ("Die k. Geschwülste," iii.). Virchow supposes that the first step is not a dilatation of the vessels, but the formation of new granulation-tissue. In this the vessels and vascular sinuses are formed. Ziegler is unable to find any traces of such a mode of genesis. He examined a liver which contained a multitude of angiomata varying from a scarcely perceptible speck to a tumor the size of a walnut. All stages of development were represented, from the dilatation of a single capillary up to the cavernous metamorphosis of an entire lobule. Yet, in no instance was there any sign of proliferation at starting; atrophy and dilatation only were observed. Payne describes a remarkable case of a similar kind in the "Trans. Path. Soc.," 1869.

The term angioma nowadays embraces formations which are genetically very diverse. Some angiomata are congenital, and are therefore conditioned by some disturbance of development. Others arise from new-formed vessels. Others, again, are the result of a kind of degenerative change; vascular dilatation following an abnormal relaxation of the vessel-wall, or on atrophy of the intervascular parenchyma. Formations of this kind, produced merely by dilatation and cavernous degeneration, should be excluded from the category of true tumors.]

151. **Aneurism by anastomosis** (anastomotic or racemose aneurism) is not properly a neoplasm; it is rather a morbid change affecting a vascular territory. The arteries of the territory become dilated and convoluted, while the intervening tissue atrophies. The pulsating growth feels to the finger like a knot of writhing worms. Many of these growths originate in congenital faults, especially those which occur in the scalp, and lead at times to erosion of the bone. Others are acquired, and follow upon mechanical injuries. The dilated arteries generally have thickened walls.

The racemose or **anastomotic varix** is analogous to the racemose aneurism. It is a common affection of the veins in the leg, the labia pudendi, and the spermatic cord (varicocele).

Further details concerning aneurism and varix will be found in the Special Pathological Anatomy, under Vascular Affections.

152. **Lymphatic angioma** (or lymphangioma) is, in relation to the lymphatic system, what angioma (as hitherto considered) is to the hæmic system. The essential character of the growth is dilatation of the lymphatic vessels, associated at times with hypertrophy of the vessel-wall and atrophy of the intervening tissue. We may distinguish the various forms into simple lymphangioma or lymphatic telangiectasis, and cavernous lymphangioma; together with a third form, the cystoid lymphangioma. As in the foregoing cases, the magnitude and arrangement of the dilatations may vary greatly. In the extreme stages actual cysts may be formed. The cavities contain lymph, which is generally clear and limpid, though it is sometimes milky.

The growth may be congenital or acquired. Congenital lymphatic dilatations take various forms according to their seat, which may be the tongue (macroglossia), lips (macrocheilia), skin (lymphatic nævus), labia, etc. Lymphangiectasis of the skin is not rare as an acquired affection; it chiefly occurs in the thigh and thorax. Sometimes it gives rise to considerable tumors, which fluctuate on palpation. The section represented in Fig. 45 was taken from a tumor as large as the fist, which had formed in the subcutaneous fat of the thigh. The dilated and sacculated lymphatics have their walls more or less thickened, and they are generally embedded in the adipose tissue.

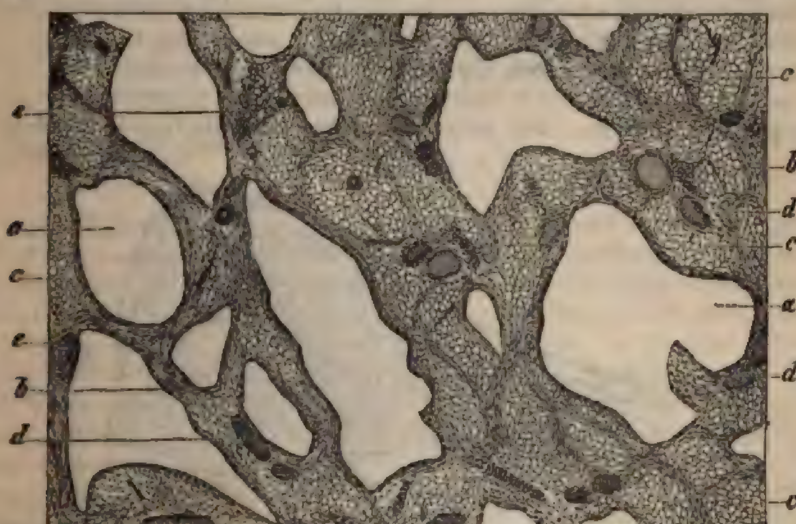

FIG. 45.—Subcutaneous Cavernous Lymphangioma. × 20 (Section mounted in Canada balsam, and stained with alum-carmine.) *a*, dilated lymphatics; *b*, connective tissue; *c*, adipose tissue; *d*, larger blood-vessels; *e*, groups of small cells or leucocytes.

If the more superficial cavities of a cutaneous lymphangioma should rupture, a grave lymphorrhœa may ensue. The affection is often complicated with fibrous hyperplasia of the skin (as in elephantiasis lymphangiectodes) or of other organs.

[References:—Maier, "Lehrb. d. allg. path. Anat.;" Virchow, *op. cit.;* Arnstein, "Virch. Arch.," vol. liv.; Anger, "Tumeurs érectiles lymphatiques," In. Diss. Paris, 1867; Gjorgewic, "Arch. f. klin. Chir.," xii.; Reichel, "Virch. Arch.," vol. xlvi.; Wegner, "Langenbeck's Arch. f. klin. Chir.," xx.; Pinner, "Centralb. f. Chir.," 12, 1880; Pospelow, "Vierteljahrs. f. Derm. u. Syph.," 1879; Hebra and Kaposi, "Diseases of the Skin" (Syd. Soc.), vol. iii.; Nieden, "Virch. Arch.," vol. xc.]

h. Myoma.

153. **Myoma** is a tumor consisting essentially of new-formed muscular fibres. It occurs only in certain parts of the body. If the fibres are

non-striated the tumor is described as a leiomyoma, if striated as a rhabdomyoma.

Leiomyoma (or levicellular myoma) is of frequent occurrence in the uterus, less frequent in the muscular coats of the intestine. It takes the form of a spherical nodulated growth, not unlike a fibroma. The smooth muscular fibres form bundles (Fig. 46), which are plaited and interwoven. They are usually surrounded by abundant fibrous tissue, which binds the fibres and the bundles together. If the fibrous tissue form a considerable part of the bulk, the tumor is described as a **fibromyoma.** Most of the uterine "fibroid" tumors are of this nature. The fibrous bands are white and lustrous, the muscular elements are pink, or reddish gray, or white. It is often by no means easy to distinguish the muscular elements from the purely fibrous. To make an exact determination, it is advisable to isolate the muscle-cells by teasing while the preparation is fresh. The isolation is easier if small fragments of the

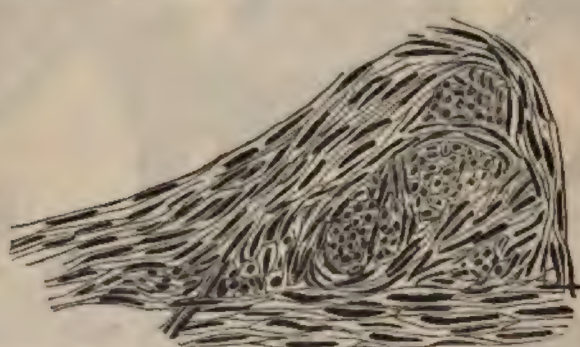

FIG. 46.—Section through a Leiomyoma (from Perls). The nuclei are shown partly lengthwise, partly cut across.

tumor have been steeped for twenty-four hours in a 20 per cent. solution of nitric acid, or for twenty to thirty minutes in a 34 per cent. solution of caustic potass. The nuclei of the muscle-cells are then easily recognized. Under the microscope the muscle-fibres are distinguished by their rod-like nuclei (Fig. 46) and by the regular structure of the tissue they form. In cross-section the muscle-spindle is seen as a small polygonal area enclosing the rounded section of the nucleus. Leiomyomata are invariably innocent; though they may cause danger by their tendency to bleed. They are liable to fatty change and to softening, which may lead to their disintegration or putrefaction, or to cystic excavations. Calcification is not infrequent.

[On the nature of so-called uterine "fibroids" see Bristowe, "Trans. Path. Soc.," 1853; Oldham, "Guy's Hosp. Rep." (2d series), vols. ii., viii.; Williams, *Lancet*, 1, 1880; Courty, "Dis. of Uterus," London, 1882 (contains full references).]

Rhabdomyomata are very rare. They are hardly ever made up entirely of striated muscular fibres. In cellular sarcomatous tumors, chiefly of the kidney and testis, spindle-cells with more or less perfect striation are found associated with smooth muscle-fibres (**myosarcomata**). It is probable that such tumors (which are found only in children, and are of great size) are due to fœtal deposits of muscular elements in the rudimental kidney and testis.

[References to the literature of rhabdomyoma are given by Huber and Boström (" Arch. f. klin. Med.," xxiii.). The name is due to Zenker ; Virchow uses the term striocellular myoma. See also Eberth, " Virch. Arch.," vol. lv.; Cohnheim, " Virch. Arch.," vol. lxv.; Marchand, " Virch. Arch.," vol. lxxiii. ; Kocher and Langhans, " Deut. Arch. f. Chir.," ix.; Brodowski, " Virch. Arch.," vol. lxvii.]

i. Neuroma.

154. **Neuroma** is a term which in strictness should be applied only to tumors composed essentially of new-formed nerve-fibres. What we are accustomed to describe as neuroma is a growth occurring indeed in a nerve, but due to multiplication of the cells of its neurilemma and perineurium, not to the formation of new nerve-fibres. It is generally a fusiform, oval, or cylindrical outgrowth, whose axis may coincide with that of the nerve, or deviate laterally. Such tumors are very often multiple, and may affect either single nerve-territories or the entire system. Neuromatous nodes may also occur in the central nervous organs ; they may be as large as a hen's egg, or (rarely) larger. If the nodular changes affect an entire nerve-territory, a network of coarse bands and nodes may be formed. This form has received the name of plexiform neuroma (Verneuil). Sometimes painful nodular growths form at the ends of divided nerves, as in amputation-stumps. They are spoken of as amputational neuromata.

Almost all of these varieties are false neuromata ; they are really fibromata and myxomata of the connective tissue of the nerve, unassociated with any multiplication of its nerve-fibres. The latter, indeed, are compressed and atrophied. This is true of the multiple varieties as well as of the amputational neuromata. The latter are in most cases due to inflammatory fibrous hyperplasia.

It is asserted, however, that, in some neuromatous tumors, a true new-formation of nerve-tissue may occur. Amputational neuromata have furnished examples of this, as well as the tumors of various sizes which develop in the continuity of a nerve without any discoverable cause. These, then, would be instances of true neuroma.

Nerve-fibres are said to multiply by subdivision and by offshoots. According as the new-formed fibres are medullated or not, we have the varieties myeline neuroma and amyeline neuroma. Neuromata are en-

tirely innocent ; they never give rise to metastases. It has been shown that the multiple false neuromata are apt to be inherited, or at least to depend on some congenital fault. (See Special Pathological Anatomy of the Nerves.)

[References :—Virchow, *op. cit.* and "Gesammelte Abhand.;" Smith, "On Neuroma ;" Perls, "Handb. d. allg. Path. ;" Verneuil, "Arch. gén. de méd.," vol. xviii. (5th series) ; Czerny, "Arch. f. klin. Chir.," xvii.; Soyka, "Prager Vierteljahrs.," 35, 1877 ; Perls, "Arch. f. Ophthalm.," xix.; P. Bruns, "Virch. Arch.," vol. l.; von Recklinghausen, "Ueber d. multiplen Fibrome d. Haut," Berlin, 1882.]

j. Lymphoma and Lymphosarcoma.

155. **Lymphoma** is a comprehensive term, and includes formations which are not strictly tumors, but rather hyperplasias of the tissue proper to lymphatic glands—lymphadenoid (or briefly adenoid) tissue, as it is called. Lymphoma, as a neoplasm, would imply the development and deposit of new lymphadenoid tissue, in the form of a tumor, within a lymphatic gland, a follicle, or some other structure of the connective-tissue group. In what is usually called lymphoma this does not happen. What does happen is—that the tissue of the lymphatic gland or follicle increases in size because the lymphoid cells it contains are multiplied, while the reticular tissue undergoes hyperplasia. The process is often inflammatory in character, and should then be classed with the inflammations ; in other cases the lymphoid hyperplasia seems to begin idiopathically, *i.e.*, without any cause hitherto discovered. It may often be doubtful whether the increased growth of a lymphatic gland should be regarded as neoplastic or as hyperplastic. Many cases of lymphoma, especially the leukæmic kinds, seem referable to hyperplasia. The lymphatic glands, lymphadenoid structures of the intestine, and lymphoid follicles of the spleen, all maintain their structure as they grow in size, or alter but slightly. Moreover, the functions of the glands seem to be more actively performed. This does not seem to indicate that they are invaded by anything of the nature of a neoplasm.

In addition to the hyperplastic lymphomata, there is a true or heteroplastic tumor whose structure agrees with that of lymphadenoid tissue. As the term lymphoma has been perverted to describe the hyperplastic formations, we may do well to distinguish the genuine tumor as **lymphadenoma** or lymphosarcoma. This latter title corresponds with the fact—that the tumor agrees in its characters with the sarcomata. It will therefore be treated in connection with them (Art. 158).

[The relations of lymphoma and lymphadenoma to Hodgkin's disease and to leukæmia are discussed in the Special Pathological Anatomy.

Recent researches have shown that lymphadenoid tissue is, in normal

conditions, widely distributed throughout the body. The overgrowth of some such normal deposit may simulate a heteroplastic formation.]

k. Sarcoma.

156. The **sarcomata** are tumors constructed on the type of the connective tissues, in which, however, the cellular constituents predominate over the intercellular substance. In this respect they resemble the immature connective tissues; so that the comparison of sarcoma to embryonic formative tissue is perfectly apt.

Sarcoma originates invariably in a structure belonging to the connective-tissue group; *i.e.*, in formed or unformed fibrous tissue, in cartilaginous, bony, mucous, lymphoid, neurogliar, or adipose tissue. The transformation of these into tumor-tissue is effected by the growth and multiplication of the constituent cells.

FIG. 47.—Section through the Advancing Margin of a small Sarcomatous Nodule from the Mamma. × 300. *a*, fibrous tissue; *b*, cells of the sarcomatous tissue; *c*, smaller cells; *d*, cells with hypertrophied nuclei; *e*, multinuclear cells.

In favorable circumstances it is possible to follow up this mode of genesis histologically. At the advancing margin of a growing tumor we may find all kinds of transitional cell-forms, from the small cells of the normal connective tissue to the large cells of the tumor. Fig. 47 represents the advancing margin of a small sarcomatous nodule from the mamma, and in it the various stages of development can be made out. Enlarged and swollen cells (*c*) lie beside the small cells of the fibrous tissue (*a*); others with enormous nuclei (*d*), or with several (*e*), are also noticeable. At the same time the number of the cells is vastly increased.

In bone and cartilage it is possible to demonstrate the subdivision and multiplication of the fixed cells even more clearly than in connective tissue. The multiplication sometimes occurs in the substance of non-vascular cartilage or bone away from the medullary spaces, and thus the part played by the individual cells within their cavities is very readily followed (Ziegler, "Virch. Arch.," vol. lxxiii.). In connective tissue it is less easy to exclude the possibility of cell-infiltration from neighboring parts. Virchow has thus shown that sarcoma-cells may arise by prolifer-

ous multiplication from connective-tissue cells of perfectly normal aspect. This is the process in a large number of cases ; but it may vary to this extent—that the development begins in tissue which is already morbidly altered. Thus new-formed cartilage may pass into sarcoma by over-intense proliferous growth of the cartilage-cells, and disappearance of the matrix-substance.

It is of great interest to note that cells, which form part of what we might call congenital heteroplastic foci, may often serve as the starting-point of a sarcoma. Congenital warts and pigment-spots are specially remarkable for this. The transformation into sarcomatous tissue is effected by the growth and multiplication of the nests of cells that are always found in such spots.

Summing up what we know of the development of sarcoma we may say—that sarcomatous tissue may arise either from connective tissues which up to then seem normal, or from tissues that are to be regarded as already morbid.

[References on the genesis of Sarcoma :—Virchow, "Die kr. Geschwülste," ii. ; R. Maier, "Allg. path. Anat. ;" Perls, "Allg. path. Anat. ;" Bizzozero, "Med. Jahrb.," iv., 1878 ; Billroth, "Arch. f. klin. Chir.," xi. ; Steudener, "Virch. Arch.," vol. lix. ; Sokolow, "Virch. Arch.," vol. lvii. ; Cornil and Ranvier, "Man. Path. Hist.," vol. i.]

157. The form and mode of growth of the cells varies much in different varieties of sarcoma. The intercellular substance is sometimes scanty, soft, and stringy ; in other cases its texture approaches that of the mature normal tissue. The various varieties are distinguished according to the constitution of the ground-substance as well as of the cells, but chiefly of the cells. That constituent is taken as characteristic, which prevails in the tumor in question. Seeing that a sarcoma is continually in process of growth, it always contains some parts which are as yet immature, and merely represent an earlier stage of development of the tumor. In settling the classification of the tumor such parts are not taken into account.

The texture of the sarcoma, as made out by the unaided eye, varies much in the different forms. In its mature condition it is generally more or less sharply marked off from its surroundings. It may occur in any locality where connective tissues are found, but the frequency of its occurrence is different in different tissues. Thus it is much commoner in the skin, fasciæ, intermuscular fibrous tissue, bone, periosteum, lymphatic glands, brain, and ovary—than in the liver, lungs, intestine, or uterus.

The amount of intercellular substance present chiefly determines the consistence and the tint. Forms which are soft, marrowy, and white or grayish-white on section, are rich in cells and poor in intercellular substance. Firm and coarse-grained forms are poorer in cells and abound more in fibrous intercellular tissue. The latter kinds pass without any

break into the fibromata. Intermediate forms are described as **fibrosarcomata.** The cut surface of a sarcomatous tumor has a uniform look throughout ; unless, indeed, it has undergone retrogressive changes, or the amount of blood in it varies from part to part. It looks evenly smooth, in medullary tumors milk-white, in firmer kinds clear grayish-white and translucent, or grayish-red or brown. The hard forms are white or yellowish-white, and lustrous on section.

The blood-vessels are variously developed ; now and then they are exceptionally wide and numerous, or even irregularly dilated, as in telangiectatic sarcoma. Lymphatics have not been shown to exist in sarcomata.

Retrogressive changes are apt to happen, such as fatty change, mucoid change, liquefaction, caseation, disintegration, hemorrhage, putrefaction, ulceration, etc.

158. **Round-celled sarcoma.** The small-round-celled sarcomata are very soft rapidly growing tumors. They chiefly occur in the connective tissues of the locomotive and skeletal system ; as also in the skin, testis,

FIG. 48.—Section through the Margin of a Sarcoma affecting the Intermuscular Connective Tissue. × 300. (Carmine staining.) *a*, normal muscle-fibre ; a_1, atrophied muscle-fibres ; *b*, round-cells intruded between the muscle-fibres ; *c*, fully developed tumor-tissue ; *d*, round-cells resembling white blood-corpuscles.

ovary, and lymphatic glands. They are usually milky white on section, and not infrequently contain softened or cheesy patches. A milky juice can be got by scraping the cut surface. Their structure is very simple ; it consists almost entirely of round-cells and vessels (Fig. 48). The former are small and fragile, have but little protoplasm, and enclose a rounded or slightly oval vesicular nucleus (Fig. 48, *c*). This nucleus seems more highly developed than it is in ordinary lymphoid cells.

The intercellular substance is scanty, and fibro-granular in texture. The vessels appear as thin-walled channels between the groups of cells. In the case of an invaded muscle, such as that in the figure (Fig. 48), the tumor seems to consist of an aggregation of round-cells (Fig. 48, *b*, *c*) seated in the intermuscular connective tissue. Lymphoid elements are not infrequently found mingled with the tumor-cells ; their nuclei (Fig.

48, *d*) are easily distinguished by the fact that they take a deeper staining than the other elements.

A second variety of small-round-celled sarcoma is the so-called **lymphosarcoma.** It is a sarcoma whose structure somewhat resembles that of a lymphatic gland. There is a kind of reticular stroma (Fig. 49, *a*), made up in part of anastomosing ramifying cells (Fig. 49, *b*); and this contains a multitude of round-cells in its meshes. If a small piece of the tumor be first shaken up in a test-tube with some liquid, so that the cells drop away, the structure can then be easily made out under the microscope.

The tumor has the same general appearance as the commoner small-round-celled variety. Both forms are highly malignant, partly because of their rapid growth, partly from their tendency to give rise to secondary growths, which may affect the entire body.

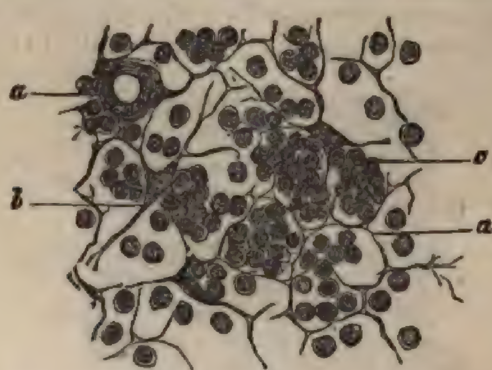

FIG. 49.—Section of Lymphosarcoma from the Nasal Mucous Membrane. *a*, reticulum (the *a* to the left points to a blood-vessel with subdividing cells); *b*, cells of the reticulum; *c*, round-cells.

Lymphosarcoma most commonly originates in lymphatic glands, and in the lymphadenoid tissue of the mucous membranes. It may, however, arise elsewhere. When it attacks a lymphatic gland, it may be distinguished from mere hyperplastic lymphoma by its rapid growth, and by its tendency to overpass the limits of the gland, and to form metastases.

159. Large-round-celled sarcomata are made up of cells considerably larger than those of the varieties just described. They occur in the same localities. They are not quite so soft in texture. Their cells are often uniformly large, and have an abundant protoplasm and large oval vesicular nuclei (Fig. 50). Many of the cells are binuclear, a few are multinuclear. The intercellular substance is arranged in a kind of network, interspersed with fusiform and ramified cells. Together they form an alveolar reticulum in whose spaces lie the large epithelium-like round-cells. On account of these characters Billroth has described the tumor as a "large-celled alveolar round-celled sarcoma." The vessels have usually very thin walls.

In the other varieties of large-round-celled sarcoma, the cells are very unequal in size. Fig. 51 represents a section of a mammary sarcoma in which the cells are for the most part round; but their sizes vary greatly, and there is a partial admixture of elongated cells, as well as of multinuclear giant-cells (*e*). If this last be taken as characteristic, the tumor may be called a giant-celled or **myeloid sarcoma** (Art. 160).

The large-round-celled sarcomata are generally less malignant than the small-celled kinds; but they likewise may form metastases. The patient from whom the tumor represented in Fig. 50 was taken died from metastatic growths.

FIG. 50.

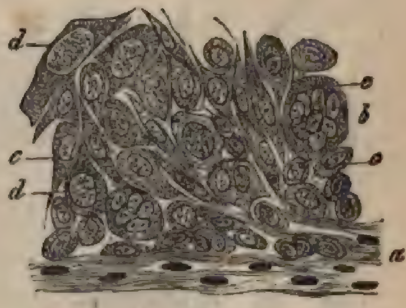

FIG. 51.

FIG. 50.—Section from a Fungating Large-round-celled Sarcoma. × 400. (From the skin of the leg; carmine staining.)

FIG. 51.—Section of a Sarcoma of the Mamma containing variously formed Cells. × 300. (Bismarck-brown staining.) *a*, fibrous tissue; *b*, cells of the sarcomatous tissue; *c*, smaller cells; *d*, cells with hypertrophied nuclei; *e*, multinuclear cells.

160. **Spindle-celled sarcoma** (including forms with ramified multiform cells, and fibrosarcoma). Sarcomata consisting of spindle-shaped or ramified cells are among the most common of all tumors. They are usually much firmer in texture than the round-celled forms. On section they look grayish or yellowish-white, and translucent; if the vessels are full of blood they may accidentally be tinged with red. They are, generally speaking, much less malignant than the round-celled sarcomata, but this depends somewhat on where they are seated.

Sarcomata in which spindle-cells predominate are called briefly spindle-celled sarcomata; they are divided into large-celled and small-celled varieties. The cells may be more or less isolated by teasing out fragments of the tumor-tissue, and in this way very long spindle-cells may occasionally be found (Fig. 52). They lie side by side in the tumor, and group themselves into bundles. In a section these bundles may be seen cut through lengthwise, crosswise, or slantwise; which shows that they run in diverse directions through the growth.

The grouping of the spindles into definite bundles is often very striking; but sometimes there is no such grouping, the spindles all lying parallel to the same direction throughout a considerable area. Sometimes

also the arrangement of the spindles seems to depend on the direction of the vessels, the bundles forming a kind of sheathing to each vessel.

The intercellular substance may be very scanty, or altogether imperceptible in a section. In other cases it is abundant, and shows a kind of fibrillated structure. The cells are then poorer in protoplasm ; so much so, in fact, that there is often none to be seen around the nucleus, and the cell-processes seem to start from the nucleus itself ("nuclear fibres"). Such tumors are firm and coarse-grained, and approach the fibromata in texture. They are called **fibrosarcomata.**

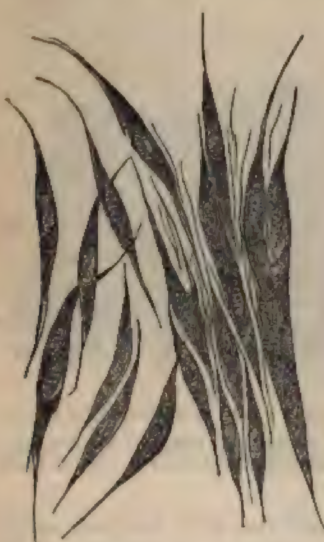

FIG. 52.

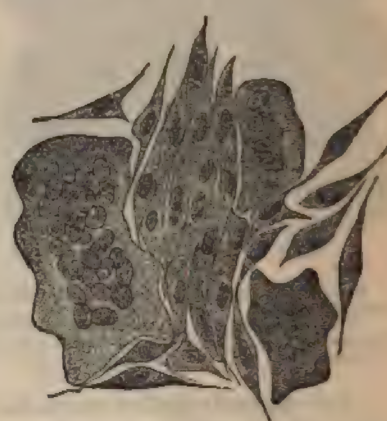

FIG. 53.

FIG. 52.—Spindle Cells from a Large-spindle-celled Sarcoma of the Cheek. × 400. (Teased preparation.)

FIG. 53.—Section from a Giant-celled Sarcoma originating in the Medulla of the Tibia ("Myelogenic" Sarcoma). × 400. (Hæmatoxylin staining.)

Sarcomata whose cells are of several diverse forms are equally common. Their cells are spindle-shaped, pyramidal, prismatic, stellate, or altogether irregular (Fig. 53). Each cell seems in fact to take the form of the space which is left to it to fill. Sarcomata of this kind, as also the spindle-celled kind, usually contain a larger or smaller number of giant-cells (Fig. 53). These tumors are perhaps more properly described as giant-celled or myeloid sarcomata than those referred to in Art. 159. They chiefly affect the osseous system.

The vessels of a sarcoma have generally walls which are quite distinguishable. In some cases, however, they have the appearance of canals excavated in the substance of the tumor, the tumor-cells themselves bounding the lumen of the vessel. Here it would seem as if the tumor had in part arisen from multiplication of the cells in the original vessel-wall.

161. **Sarcomata of peculiar types.** Sarcomata do not usually exhibit any special structure, or any resemblance to a glandular type. The cellular elements, even when they seem to resemble epithelial cells, are dispersed uniformly throughout the intercellular substance, as in the connective tissues. There are, however, exceptions to this in special cases. There are sarcomata which have a structure resembling that of gland-tissue, or of epithelial new growths. This appearance of structure is due in part to the epithelial look of the cells, but chiefly to their aggregated arrangement in groups separated by fibrous septa. Such tumors are described as **alveolar sarcomata.** Fig. 54 represents a section from an alveolar sarcoma of the skin.

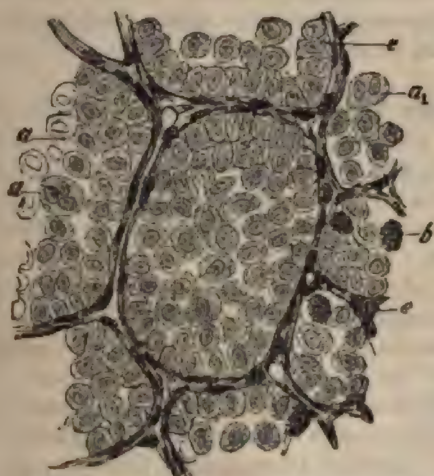

FIG. 54.—Section from a Melanotic Alveolar Sarcoma of the Skin. × 300. (Hæmatoxylin staining.) a, uninuclear; a_1, multinuclear epithelial-like tumor-cells: b, pigment-cells; e, stroma enclosing blood-vessels and pigment.

The cells a exactly resemble epithelial cells; they are grouped into masses, and sharply distinguished from the fibrous framework (e) in which they are embedded. This latter contains the blood-vessels, or rather the framework is chiefly made up of a network of blood-vessels; but no vessels enter the cell-groups. This is another point of structure in common with the epithelial growths.

Tumors of this kind occur chiefly in the skin, but they are also met with in the bones, lymphatic glands, and pia mater. In the case of the skin they originate in warts and pigment-spots, which generally contain such groups or nests of cells (Arts. 156 and 398).

The way in which the alveolar structure is developed can often be clearly made out, especially in tumors of the central nervous system. The normal intervascular tissue is transformed into masses of sarcoma-cells, while septa are formed between the cell-masses by the fibrous tissues lying along the course of the vessels. In other cases it looks as if

a plexus of pre-existing or new-formed vessels took on, as it were, an investment of cells, and this grew thicker and thicker, till at length the intervascular spaces were entirely filled up. Accordingly we find this form of growth described as plexiform angiosarcoma. It has also been described, and not infrequently, as **endothelioma**. On this view the cell-nests arise by proliferation from endothelial cells. This certainly happens when masses of cells are formed from the endothelial covering of the subarachnoid meshwork and pia mater; the masses afterward group themselves into "nests." Sometimes the proliferous endothelial cells of the pia mater are aggregated into small spherical nodules of a peculiar lustrous appearance. The tumor into which the membrane is transformed then contains small shining pearly bodies, made up of laminated layers of squamous or tabular cells. Such tumors have been called **cholesteatomata,** or pearly tumors.

[The expression "plexiform angiosarcoma" is due to Waldeyer ("Virch. Arch.," vol. lv.). The vessels of the brain, lymphatic glands, serous membranes, and testis possess what is called a perithelium; that is, the adventitia is invested with endothelial cells. Proliferation begins in the cells of this perithelium, and the vessel is thus invested with a stratified covering. See Kolaczek, "Deutsche Zeitsch. f. Chir.," ix.; Maurer, "Virch. Arch.," vol. lxxvii.; Neumann, "Arch. d. Heilk.," 1872; Klebs, "Prager Vierteljahrsschr.," 1876.

[It is still a matter of dispute whether the cholesteatomata are really endotheliomata of the pia mater (Eppinger, "Prager Vierteljahrsschr.," 1875). They may possibly belong rather to the dermoid tumors (Art. 178). Similar growths are met with in the middle ear (Wendt, "Arch. d. Heilk.," 14, 1873; Lucæ, "Arch. f. Ohrenheilk." (New Series), 1, 1874.) Some regard them as tumors, others (with Wendt) as inflammatory products.]

162. Sarcomata which contain deposits of pigment are described as **melanosarcomata** (Fig. 54). The pigment is black or brown, and lies partly in the tumor-cells, partly in the fibrous matrix and vessel-walls. It occurs chiefly in the form of amorphous granules; but there are generally a number of diffusely stained cells as well. Melanosarcomata are malignant.

When the pigmentation is not extreme the tumor has on section a brownish-gray look, or it may only show patches of brown or black. In more marked cases the section is uniformly black. Very often the secondary growths are more intensely pigmented than the primary tumor, and this is also the case in growths that have recurred after resection. Tumors of this kind develop in tissues like the eye and pia mater, which normally contain pigment-cells, or in pigmented pathological formations. The black pigment-spots (melanomata) of the skin are of this latter class; it has already been mentioned that they contain peculiar clusters or nests of cells (Fig. 54).

We do not know in what way the pigment is formed (Art. 67). It is not to be confounded with the brown pigment derived from extravasated blood. Patches stained with this blood-pigment are sometimes found here and there in a sarcomatous growth, but the true melanotic pigment is something quite distinct.

Psammomata, like melanosarcomata, are growths which arise in certain definite tissues, and but rarely anywhere else. They are sarcomatous, fibrous, or myxomatous tumors originating in the brain and its membranes, more particularly in the choroid plexus and pineal gland, and containing a multitude of chalky concretions. These have the same structure as the grains of the normal brain-sand (*acervulus cerebri*). They are made up of concentric calcareous strata, and form spherical or dendritic aggregations. They may be so abundant as to give the tumor a stony feel.

[We may here just mention the variety of sarcoma called **chloroma.** It is a cellular tumor, whose section has a light green or dirty brownish-green tint. The color soon fades on exposure to the air. Nothing is known of the nature of the coloring-matter. Chloromata occur chiefly in the periosteum of the skull. See Huber, "Arch. d. Heilk.," 1878.]

163. Some very peculiar forms of tumor are produced when sarcomatous tissue undergoes partial hyaline or mucoid degeneration ; or when sarcomatous and myxomatous formations combine. They are generally included under the term **cylindroma,** though this may also be applied to tumors of another species in which epithelial cells are involved (Art. 173, Fig. 72).

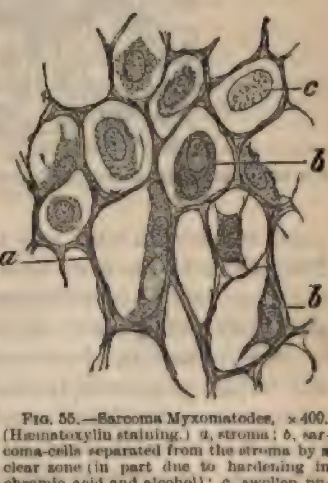

FIG. 55.—Sarcoma Myxomatodes, ×400. (Hæmatoxylin staining.) *a*, stroma ; *b*, sarcoma-cells separated from the stroma by a clear zone (in part due to hardening in chromic acid and alcohol) ; *c*, swollen nucleus which has lost its protoplasm.

The ordinary soft cellular sarcomata have now and then a more translucent appearance than usual, and yield on section a turbid slimy juice. These have already begun to undergo mucoid change, as may be recognized by the swollen appearance of the cells, and the formation of drops of liquid within them. When the tissue has been hardened the change is not so easily made out. The cells then seem shrunken (Fig. 55, *b*), and separated from the stroma (*a*) by a clear zone. Sometimes a few distended and transparent nuclei are observed, their protoplasm having become mucoid and so vanished.

This mucoid change may at times extend throughout the entire substance of the tumor ; or it may be confined to scattered patches, separated by unchanged cells. Isolated hyaline spherules are occasionally

noticed among the cells. Such partially degenerate sarcomata we may describe as **myxomatodes.**

The tumors in which sarcomatous and mucous tissue are found combined have on section either a hyaline or an opaque dirty white appearance. The mucous tissue is partly composed of a network of ramified and anastomosing cells (Fig. 56, *a*), in addition to a mucoid basis-substance. Within this tissue lie also branching clumps and strings (*b*) made up of closely compacted cells. These strings are very irregular in form and anastomose in all directions; they give the tumor a very peculiar texture. Its general structure justifies the name of **myxosarcoma,** which has been applied to it. It forms, as has been said, a subdivision of the class of cylindromata. It is not clear, from a histological

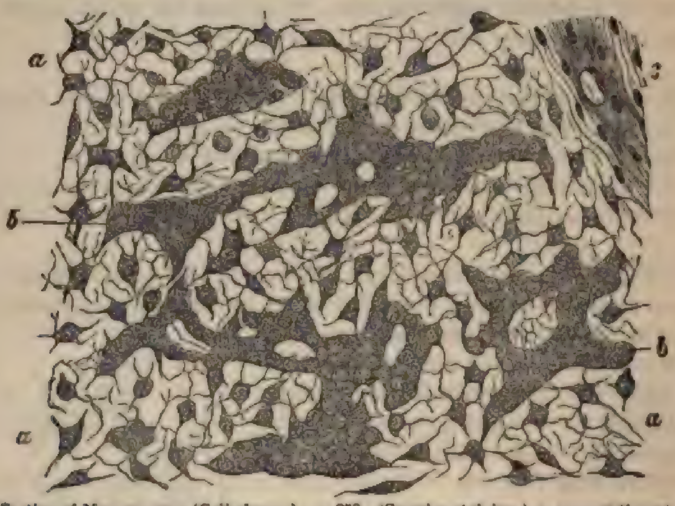

FIG. 56.—Section of Myxosarcoma (Cylindroma). × 250. (Carmine staining.) *a*, mucous tissue; *b*, strings and clumps of cells; *c*, fibrous tissue.

point of view, in what way the clumps and strings of cells are formed. They seem to have no relation to the ramifications of the vessels, for these are seen to be unchanged, and run through parts where the fibrous tissue has undergone no degeneration.

A third variety of cylindromatous tumor, also somewhat translucent and in part gelatinous, is characterized by the hyaline degeneration which affects the walls of its vessels and the tissue around them. If one of these vessels be isolated, it is seen to be invested with a more or less abundant deposit of hyaline substance (Fig. 57, *a*). To this sheath are attached similar hyaline appendages not traversed by vessels. Outside the hyaline sheaths, alternating with them in fact, are nests and strings of cells which here and there seem fastened or anchored to the hyaline masses (Fig. 57, *b*). The strings of cells have much the same look as those shown in Fig. 56, and we infer that the tumor in question is allied to the myxosarcomata just described. The homogeneous appendages are

the result of hyaline degeneration of the vessel-walls, or of the neighboring tumor-cells ; and this hyaline degeneration is either identical or connected with mucoid degeneration. The fact that actual mucous tissue (like that in Fig. 56) is occasionally found mingled with the hyaline masses tells in favor of this view.

This form of cylindroma may therefore be regarded as a peculiar variety of myxosarcoma, in which the mucoid change is chiefly confined to the vessels, and in which the formation of new vessels is an essential feature. To emphasize the important part played by the vessels in this neoplasm, we might call it **angiosarcoma myxomatodes.**

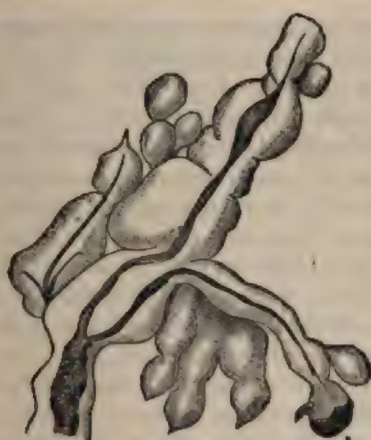

FIG. 57.—Blood-vessels with Hyaline Sheath and Appendages from a Cylindroma. × 200. (From Sattler's "Cylindrome," 1874.) *a*, small vessel ; *b*, patch of epithelial-like cells on one of the hyaline appendages.

Such growths have been found principally in the lachrymal glands, salivary glands, and in the brain. They occur, however, elsewhere, as in the lip, placenta, adipose tissue, etc.

[Cylindroma is a term due to Billroth ("Untersuch. über die Entwick. d. Blutgefässe," 1856). Such tumors, characterized by gelatinous masses and reticula, have since then been very variously interpreted. Köster described them as cancroids ("Virch. Arch.," vol. xl.); Sattler ("Ueb. d. sogen. Cylindrome," Berlin, 1874) as alveolar sarcomata, in which the cell-masses derived by proliferation from the adventitia had been transformed into hyaline cylinders; Ewetzky ("Virch. Arch.," vol. lxix.) as plexiform angiosarcomata with hyaline degeneration of the fibrous stroma, or of the adventitia of the vessels. R. Maier ("Virch. Arch.," vol. xiv., and "Lehrb. d. allg. path. Anat.") found cylindromata in the placenta and dura mater ; he regarded the presence of an abundance of hyaline mucous tissue persisting for a long period unchanged as characteristic of the tumor. This tissue may develop out of cells or out of intercellular substance, fibrous tissue, cartilage, or tunica adventitia.

Various tumors have been described as cylindromata which certainly do not all belong to the same species. A number of them belong to the sarcomata. Within this group we may, as we have said, distinguish two main forms: first, the combined sarcoma and myxoma, and secondly, the sarcoma with hyaline or mucoid degeneration extending to the cells, but chiefly affecting the sheaths of the vessels. Between these two, however, many transitional forms are found.]

l. Mixed Tumors of the Connective-tissue Group.

164. We have already referred to various tumors in which combinations of different tissues present themselves. In one sense, no tumor can be said to consist of a single kind of tissue only. In a new growth of any size we must always have new vessels, for instance. And tumors whose characteristic element is not fibrous tissue—such as chondromata, osteomata, sarcomata, myomata, and myxomata—always contain a very considerable quantity of fibrous tissue as an accessory.

We do not speak of such cases as examples of mixed tumors, because the accessory tissue is, as it were, put out of sight by the characteristic element; it is entirely subordinate. But if the second tissue comes into the foreground and affects the texture of the growth in a perceptible way, we must indicate this in our terminology. This is done by applying to the name of one neoplastic tissue the name of the other as a qualifying term; or by simply combining the two names into a compound word. Thus, as in gliomata and fibromata, the blood-vessels may be remarkable by their abundance, size, and dilatations; we then speak of the growth as a glioma (or fibroma) telangiectodes or cavernosum. A morbid combination of adipose tissue with mucous tissue is called lipoma myxomatodes or lipomyxoma; a combination of cartilage and sarcoma—chondrosarcoma; and so on. It is not rare for three or more kinds of neoplastic tissue to be found within the same tumor. A growth which starts in fascia or intermuscular fibrous tissue may consist, for example, of fibrous, sarcomatous, mucous, and adipose tissue; there may even be vascular changes here and there which give it a telangiectatic character. Such a combination is not very surprising. The neoplastic proliferation may itself result in the development of several diverse tissues—or, what is more common, the tissues of the connective group become transformed the one into the other. We showed, for example, in Arts. 90–92, that cartilage readily passes into mucous tissue, which is also frequently produced from fibrous or adipose tissues. Sarcomatous tissue may easily be the result of proliferation of the cartilage of a chondroma, or the fibrous tissue of a fibroma; and conversely, sarcomatous tissue may equally well be transformed partially into osseous tissue. Tumors originating in bone are very apt to show a tendency to bone-formation. There are two forms pecesially in which this often occurs—namely, osteoid chondroma, a com-

bination of cartilage and bony tissue; and osteosarcoma, a combination of sarcoma and bony tissue.

165. **Osteoid chondroma** (or osteochondroma) chiefly affects the larger long bones. If no sarcomatous proliferation has modified it, it usually forms a hard tumor seated on the bone or embracing it. It often reaches an enormous size; and cannot be cut with the knife, unless a patch of unaltered cartilage be hit upon. When sawn through, the cut surface has the look of dense, white, continuous bone; on closer examination this is seen to be interspersed with streaks and islands of more translucent cartilage. Fig. 58 shows well the general texture of the growth and its

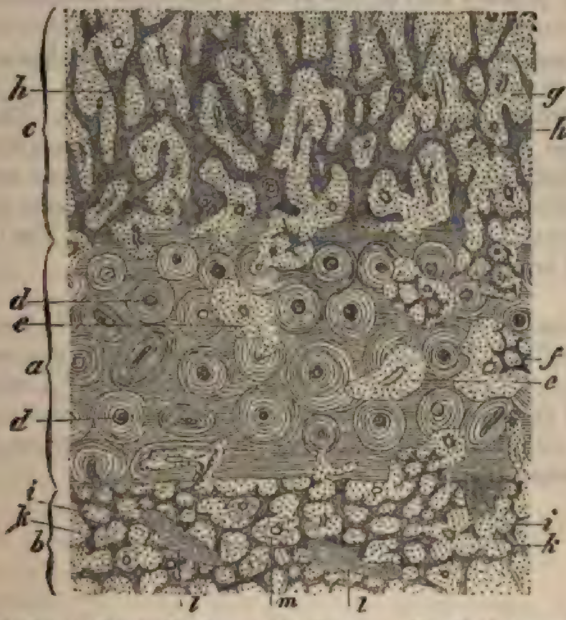

FIG. 58.—Section from an Osteoid Chondroma of the Humerus. (Magnified by means of a simple lens; double-staining with hæmatoxylin and carmine.) *a*, cortical layer; *b*, medullary spaces or cancelli; *c*, periosteal growth; *d*, normal Haversian canals; *e*, Haversian canals distended with cartilage, which at *f* contains a core of new bone; *g*, cartilage developed from periosteum, which at *h* contains bony trabeculæ; *i*, cartilage developed from medullary tissue, which at *k* contains bony trabeculæ; *l*, original trabeculæ; *m*, remnants of medullary tissue.

matrix, and its relation to the bone. The section represented is taken from a tumor of the humerus. The tumor was very firm and bony, and surrounded the bone so as to double its diameter. It was found on dividing the bone longitudinally that the medullary spaces were filled with firm tumor-tissue of the same structure as the periosteal growth. The original bone was only recognizable in the region of its cortical layer. Fig. 58 represents a section taken at right angles to the axis of the bone, and including the periosteal growth, the cortical layer, and a part of the altered cancellous tissue.

We find instead of periosteum a mass of cartilaginous tissue (*g*) in-

terspersed thickly with bony trabeculæ (*h*). These run generally at right angles to the surface of the original bone, but anastomose freely. Small lacunæ and canals are seen throughout the cartilage; they contain a few blood-vessels and a small amount of fibrous tissue. The cortical layer (*a*) is still distinguished by the concentric stratification of the lamellæ. Many of its Haversian canals are dilated and filled up (except for a small lumen in which the blood-vessel runs) with masses of cartilage. These masses sometimes contain trabecular cores of new-formed bone (*f*). Instead of the marrow, which should fill the interior of the bone (*b*), we find vascularized cartilage, also containing numbers of trabeculæ. The genesis and primary seat of the growth may thus be made out at once from this preparation. Cartilaginous proliferation has been set up in the periosteum and in the medullary tissue, and the product has subsequently been partially transformed into bone.

Osteosarcoma has an exactly analogous appearance. The difference is merely that sarcomatous tissue fills the spaces between the trabeculæ instead of cartilage. The trabeculae are at the same time more delicate and less numerous. The seat of the tumor (as is the case too with osteoid chondroma) is often confined to the periosteum. The bone is then more or less eroded.

[References:—Müller, "Müller's Arch.," 1843; Virchow, "Die kr. Geschwülste," i.; Rindfleisch, "Path. Hist.," ii.; Wilks and Moxon, "Path. Anat.," London, 1875; Paget, "Surg. Path.," Lecture 33. A summary of cases and some beautiful drawings of sarcomatous tumors connected with bone will be found in Butlin's "Sarcoma and Carcinoma," London, 1882.]

CHAPTER XXVII.

EPITHELIAL TUMORS.

166. The tumors we have hitherto treated of have been developed out of tissues belonging to the connective-tissue group; in other words, out of tissues derived from the mesoblast. The tumors we have now to deal with contain in addition **epithelial elements,** that is to say, structures derived from the epiblast and hypoblast. These epithelial elements are in fact the structures which give its special character to the class. The tumors of the class are therefore very fitly comprehended under the one title of epithelial neoplasms. All of them consist of epithelial cells on the one hand, and of vascular connective tissue on the other. The latter tissue goes to form the framework or stroma in which the epithelial elements are embedded. The type or plan of their construction is that of the simple gland, and they maintain the resemblance throughout many of the phases of their development. They thus call to mind in many ways the various glands of the body; though the degree of resemblance differs much in the different forms.

Some of them are built exactly on the plan of some particular gland; the new-formed tissue corresponds to a definite glandular type. Tumors of this kind we call **adenomata.**

Another group never reach this perfection of structure. They exhibit as it were only the first stage of the gland-making process. Epithelium and fibrous tissue interpenetrate each other in an inchoate way. The process is never carried higher, but the crude formation is repeated and reproduced indefinitely. By multiplication of the epithelial cells we have produced nests and clusters and strings of cells, and these are embedded in connective tissue whose elements are likewise multiplying. The result is a neoplasm consisting of a fibrous network or framework, in the meshes of which are lodged a multitude of variously shaped epithelial cells. But there is no orderly arrangement of these epithelial cells. In the adenomata they tend to clothe the walls of the alveoli in a regular way, leaving open a central lumen as in the acinus of a gland. In the tumors now considered these cells remain in compact irregular masses. Epithelial tumors of this kind, in which the glandular type is most imperfectly followed, are described as **carcinomata** or true cancers.

Adenoma and carcinoma are generally malignant. They tend to in-

vade the surrounding tissues; and, by the channels of the lymph or of the blood, are apt to affect distant regions and produce metastases. But the degree of malignancy varies greatly; it depends not only on the histological structure of the growth, but, to an even greater extent, on its locality.

[The definition we have given of adenoma and carcinoma is based partly on their histology, partly on their mode of genesis. From the morbid anatomist's point of view this is the only correct mode of definition. Tumors containing none but mesoblastic cells may and do correspond in their general structure with others, in which undoubted epithelial cells form the characteristic element; and for this reason a merely anatomical method of diagnosis would be insufficient. If carcinoma be defined as an alveolar tumor composed of a fibrous network containing nested cells, it is impossible to separate between carcinoma and alveolar sarcoma. It is owing to this purely anatomical mode of definition that we have had controversies as to whether carcinoma really depends upon epithelial proliferation, and whether cancers may not have their origin in fibrous structures. Such controversies become irrelevant if we base the distinction on histogenetic grounds. A tumor is to be called carcinomatous only when the epithelial elements take an active part (as above described) in its formation. A connective-tissue tumor which has ostensibly the same structure, but whose mode of genesis is entirely different, is to be distinguished as an alveolar sarcoma.]

a. Adenoma.

167. **Adenoma** is a tumor constructed after the type of a secreting gland. The definition might at first sight tempt us to term every glandular enlargement, in which the elements are abnormally multiplied, an adenoma. This would, however, be incorrect. Adenoma is a true neoplasm, characterized physiologically by its impotence to produce the normal gland-secretion, and anatomically by its want of relation to the tissue in which it is seated. A gland enlarged by overgrowth, or overwork, or chronic inflammation, cannot be described as an adenoma. It is a hyperplasia; and if it be the true gland-tissue and not merely the fibrous framework which is excessively developed, the physiological activity of the gland is thereupon increased.

We must regard in the same way the tumor-like growths which occasionally develop in mucous membranes, chiefly as a result of chronic inflammation. They are mere localized proliferations, rising above the general surface as nodular, polypous, or papillary outgrowths. The fibrous tissue is the first to increase, and this leads to some increase of the epithelium, chiefly because the local submucous swelling involves an increase of the mucous surface. If any glands are present (as in the intestine or uterus), they also undergo change. If their ducts become

blocked, they may become distended with secretion, and form larger or smaller cysts. Other glands may enlarge by increase of their stroma; and lastly, there may be in some an active growth and increase of the specific gland-tissue.

It is easy to demonstrate that such new-formations of fibrous and glandular tissue do take place. The most suitable objects for examination are perhaps the papillary or villous growths which form on the inner surface of glands undergoing cystic degeneration (Fig. 59, *c*). These are sometimes so abundant that the cyst seems quite filled up with the new tissue.

FIG. 59.—Papillary Growths inside a Cyst. × 300. (From a gastric polypus: hæmatoxylin staining.) *a*, gland tubules with cylindrical epithelium; *b*, stroma infiltrated with cells; *c*, papillary growths into a cyst, covered with mucoid epithelium.

Such an overgrowth of the mucous membrane, in which the local glands are simultaneously enlarged, is best described as a glandular hyperplasia.

168. True adenoma is generally distinguishable from glandular hyperplasia by obvious characteristics. Its consistence, color, and structure all mark it off plainly from the surrounding tissue.

Adenomata are usually knot-like growths arising within the substance of glands, or in glandular epithelial or epidermic tissues. In the first case it is generally a part only of the gland that is transformed into tumor-tissue. In the mucous membranes and skin the tumor is likewise circumscribed. When an entire organ like the ovary is included in the growth, it is easy to make out by the alteration in the structure that it is an adenoma, and not the result of simple hypertrophy. Adenomata are often pale, soft, and marrowy; in other cases they are dense and coarse.

Microscopic examination will obviate any doubt, which mere inspection may leave, as to the nature of a questionable adenoma. The structure of the neoplasm is always different from that of the affected tissue. It always corresponds with the type of some normal tissue; but this is not the type of the matrix in which it lies. Adenoma of the intestine may be made up of ramified and convoluted tubules—not of Lieberkühnian crypts. Adenoma of the liver may be made up of tubular glands instead of lobules. Adenoma of the mamma is at once distinguished from the normal gland-tissue by the mode in which the epithelial cells are reproduced and arranged, and by the structure of the neoplastic acini.

The difference between normal and neoplastic gland-tissue is perhaps most marked of all in the case of the ovary. Ovarian adenoma is apt to grow to an enormous size, and very often imperils the life of the patient afflicted with it. It usually takes the form of a multilocular **cystoma**, or cystadenoma, as it is called, and is made up of a multitude of small and large cysts. These contain a ropy, clear or turbid, and variously

tinted liquid. Their inner surface resembles that of smooth mucous membrane. The walls are chiefly of a fibrous texture; but here and there occur masses of tissue with a soft marrow-like section, and white or pink in color, which resemble parenchymatous gland-substance. These masses exemplify the early stages of the tumor's development; they consist of a fibro-cellular stroma, containing glandular tubules lined with tall cylindrical epithelium (Fig. 60). Some of the tubules are dilated. This dilatation is the first step toward the formation of a cyst; it is the result of an accumulation of secretion. When small cysts are thus formed, the fibrous tissue round them often proceeds to grow into the cavity in the form of papillary protuberances (Fig. 60). These papillary growths, which often develop in vast numbers, give to this variety its specific name of papilliferous cystadenoma.

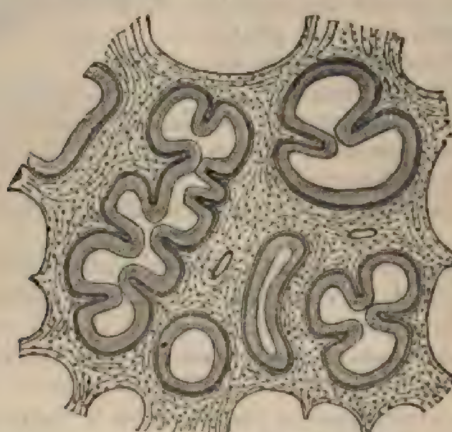

FIG. 60.—Section from a Papilliferous Cystadenoma. × 40. (Hæmatoxylin staining.)

169. All adenomata have not the same grave significance, whether we regard the affected organ or the system generally. Ovarian adenoma destroys the organ and jeopardizes life by its size; but it forms no metastases and does not invade neighboring structures. Adenoma of a sweat-gland or sebaceous gland remains as a local tumor, never reaching any great size. But the case is different with the adenomata of the alimentary canal, namely those of the stomach, large or small intestine, and rectum. Each of these tends to invade and destroy the surrounding parts, and to form metastases. They are as malignant as the malignant carcinomata. In order to indicate this fact in their distinctive name, they have been called destructive adenomata, or **adenocarcinomata.** Their malignancy is manifested even in their local behavior. Fig. 61 represents a section through the advancing margin of a small destructive adenoma of the stomach; it is remarkable for the great size of its glandular tubules and of the epithelial cells which line them.

The figure (Fig. 61) shows that the neoplastic tubules are first devel-

oped in the mucosa, the normal constituents of the mucous membrane simultaneously disappearing. Starting thence the neoplasm invades the submucosa (*b*). It intrudes itself along the intermuscular septa between the muscle-bundles of the muscularis (*c*); and finally extends along the serous layer (*d*). Here and there through the fibrous tissue may be seen heaps of small cells; this indicates that proliferation is going on in this tissue likewise.

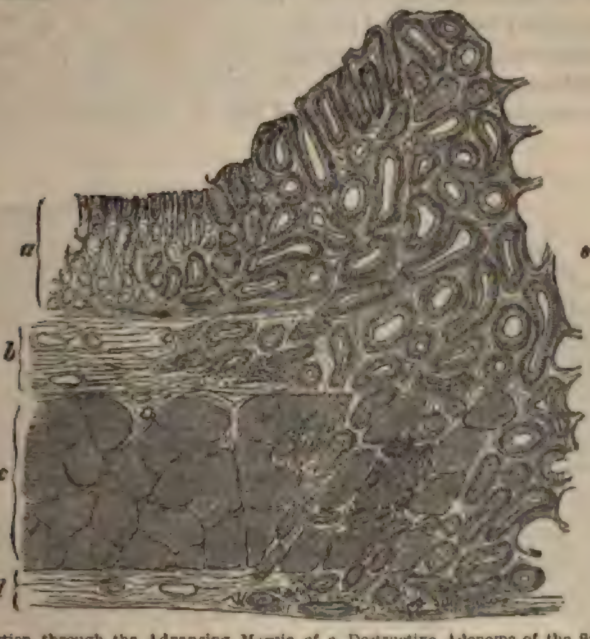

FIG. 61.—Section through the Advancing Margin of a Destructive Adenoma of the Stomach. × 25. (Hæmatoxylin staining.) *a*, mucosa; *b*, submucosa; *c*, muscularis; *d*, serosa; *e*, neoplasm which, starting from the mucosa, has invaded the other layers. Small-celled infiltration here and there accompanies the formation of the neoplastic tubules.

This invasion of the neighboring tissues is the first step toward the formation of metastases. Clearly the lymph-spaces of the tissue are certain to be encountered by the advancing growth, and when this happens the path of infective transport stands open.

Destructive adenoma is a soft marrowy tumor, taking the form either of a papillary or fungous outgrowth, or more commonly of a level and extensive thickening of the mucous membrane. The new tissue frequently breaks down and ulcerates. The ulcers have a soft infiltrated base and raised rampart-like edges, or the surrounding tissue is beset with nodular growths.

b. Carcinoma.

170. If we define **carcinoma** as a growth characterized by epithelial multiplication (Art. 166), and not agreeing with any normal glandular type, we must at the same time lay stress on the fact that this epithelial

multiplication is no merely accessory or subordinate feature. It is the essential and distinguishing character of the neoplasm.

Simple non-typical multiplications of epithelium are by no means uncommon ; but they are not necessarily to be interpreted as carcinomatous. Subepidermic granulomatous tumors of the skin (Art. 132, Fig. 37) will often exhibit in their superficial layers clusters and rolls and strings of epithelial cells altogether diverse from any normal mode of grouping ; and the same may be observed in skin-wounds which are in process of repair by epidermic growth and multiplication. So, too, in glands altered by inflammation, and in fibrous tumors occurring in glands, the glandular epithelium may begin to multiply and lead to the formation of epithelial

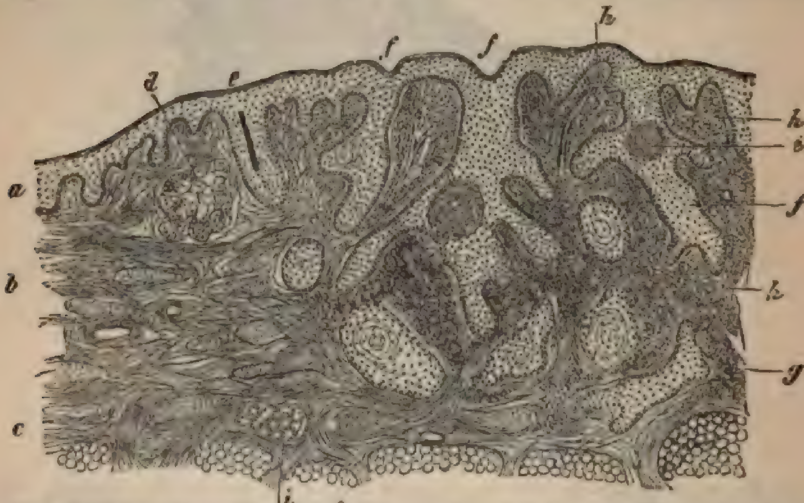

FIG. 62.—Section from a Cutaneous Cancer or Epithelioma. × 20. (Aniline-brown staining.) *a*, epidermis ; *b*, corium ; *c*, subcutaneous areolar tissue ; *d*, sebaceous gland ; *e*, hair-follicle ; *f*, cancerous ingrowths from the epidermis ; *g*, deep-set cancerous cell-groups ; *h*, proliferating fibrous tissue ; *i* (*above*), cell-nest or epidermic globe ; *i* (*below*), sweat-gland.

masses that are altogether non-typical or atypical in appearance. Formations of this kind are not to be classed with the carcinomata. They lack the power of growing indefinitely and of infiltrating the surrounding tissues. They are incapable of raising themselves to the rank of the independent tumor, that is nourished like a parasite at the expense of the organism, and invades the tissues to their destruction. They can only extend where a free surface is open to them, due either to antecedent inflammation or to the formation of a true tumor. In wounds or subepithelial granulations these proliferous growths have no more significance than the covering of an abraded surface with new epithelium. The epithelium forms only in places where the underlying tissue is so arranged as to leave free surfaces or open fissures, and the process amounts, in a word, merely to the "skinning-over" of internal surfaces.

The mode in which true carcinoma develops and extends is quite dif-

ferent. The epithelial new-formation is not limited to free or bared surfaces; it actively invades the contiguous connective tissues. Thus we may have a cutaneous cancer or epithelioma, which consists essentially of cellular prolongations of the interpapillary promontories of the Malpighian layer, penetrating and ramifying in the fibrous tissue of the corium (Fig. 62, *f*). These prolongations go on growing and multiplying, and ultimately infiltrate the corium over a more or less extensive area, taking the form of detached strings and nests of cells (*g*). In this case, then, we may regard the carcinoma as an epithelial infiltration of the corium starting in the superficial epidermis. The share taken by the corium itself is not always the same. At first we are generally unable to detect in it any histological change whatsoever. The fibrous stroma in which the epithelial cells are lodged is furnished by the unaltered corium alone. In other cases, and in later stages (Fig. 62, *h*), a perceptible amount of cell-multiplication, and occasionally of vascularization, takes place. It almost looks as if the fibrous tissue were endeavoring, by compensatory growth on its own part, to counteract the invasion of its borders by the epithelium.

In tumors formed in the way we have described, the intruded masses of epithelial cells are spoken of as **cancerous cell-nests**, and the separate cells as **cancer-cells**. The fibrous framework in which they lie, made up partly of pre-existing and partly of new-formed fibrous tissue, is called the **cancerous stroma**.

171. The development of cancer in glands is essentially similar to that which starts in squamous epithelium or epidermis. Thus in the glands of the uterus we have cancer commencing with active growth and multiplication of the cylindrical epithelial cells. The single layer of cylindrical cells is transformed into a series of stratified or disorderly masses of epithelium (Fig. 63) piled upon each other. The size of the gland (*b*) is thus considerably increased, and soon its typical structure is overlaid and lost by the substitution of great cell-masses and cancerous cell-nests or loculi. The cells retain their cylindrical form only at the borders of these groups. This represents the first stage. In the second, the surrounding tissue is invaded and infiltrated by cancerous cell-nests.

A section from the advancing margin of a mammary cancer (Fig. 64) shows at one view the various steps of the process; a low magnification is all that is necessary. The first stages in the formation of the mammary cancer are essentially the same as those observed in uterine cancer, though the peculiarities of the matrix bring about certain minor variations. The primary aberration is an excessive multiplication of the glandular epithelium. This is followed by general epithelial infiltration. The small and scattered acini of the mamma are replaced by cancerous cell-nests of various form and size (*e*), embedded in a scanty stroma. Starting from these as primary foci, the infiltration of the connective tissues (*g*, *f*) extends far and wide beyond the region of the gland-tissue itself. The fibrous bundles are thrust asunder by the multiplying cells, which link

themselves into fusiform or rounded masses, or into long ramifying strings and bands. Spreading upward these invade the corium; single cell-nests may even be found immediately underlying the epidermis (*g*). Within the substance of the nipple (*a*), also, we may discover numerous cancerous patches (*h*) in the fibrous tissue between the galactophorous ducts (*d*). In the figure we note that the only uninvaded part of the gland is near its edge. Even here, however, the groups of round-cells scattered through the connective tissue (*k*) show that the structures are not altogether in their normal condition.

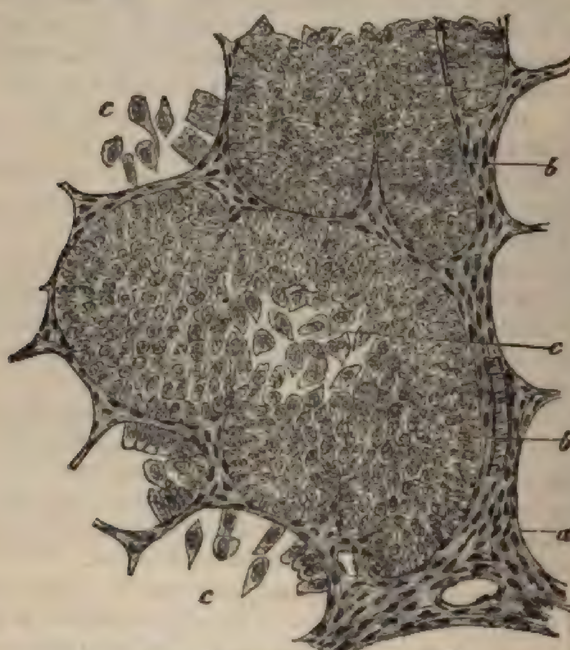

FIG. 63.—Section from a Cancer of the Uterine Glands. × 250. (Hæmatoxylin staining.) *a*, stroma; *b*, cancerous ingrowths or loculi; *c*, isolated cancer-cells.

To sum up all that we learn from this preparation concerning the extension of the cancer we may say—that the process consists in infiltration of the connective tissue with epithelial cell-nests; that this is accompanied or succeeded by inflammatory or proliferous changes in the connective tissue; and that these ultimately result in fibrous hyperplasia.

[We are chiefly indebted to Thiersch ("Der Epithelialkrebs," 1865) and Waldeyer ("Virch. Arch.," vols. 41, 55) for the discovery that a large class of tumors (other than the adenomata) existed, in which epithelium formed an essential constituent. Thiersch demonstrated that cancer-cells are derived from epithelium, drawing his arguments principally from cases of cutaneous cancer or epithelioma. Waldeyer extended his

researches to organs of every kind. Many subsequent observations have proved—that a considerable number of tumors which were believed by Virchow and others to originate as connective-tissue growths do really originate in epithelial growth and multiplication. The class of connective-tissue tumors has thus been greatly diminished. The great majority of the alveolar tumors included by Virchow under the general term carcinomata must now be ranked as epithelial tumors. See Billroth's "Surg. Pathology," third edition; Lücke, in "Billroth u. v. Pithas Handbuch," vol. ii.; Schrön, "Contrib. alla anat. della cute umana," 1865; and, for criticism of the "epithelial theory" of carcinoma, Paget's

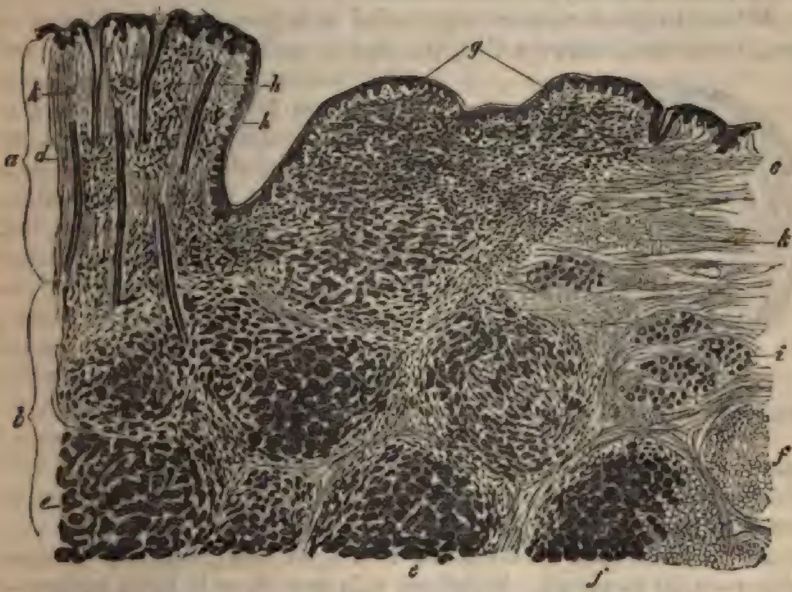

FIG. 64.—Section through a Mammary Cancer. (Magnified by means of a simple lens.) *a*, nipple; *b*, mammary tissue; *c*, skin; *d*, galactophorous ducts; *e*, cancer-tissue replacing the gland-tissue; *f*, fat-lobules, normal or undergoing cancerous change; *g*, cancerous skin; *h*, cancerous cell-nests in the nipple; *i*, normal acini; *k*, infiltration of fibrous tissue with round-cells.

"Surg. Path.," Lect. 35. Köster's attempt ("Die Entwickelung der Carcinome," 1869) to disprove the participation of the epithelium in a large class of alveolar tumors, and to derive the cell-nests from the proliferous endothelium of the lymphatics, has not proved successful.

This being the case, it will be best in future to designate the various tumors not according to their structure merely, but also with respect to their genesis. Carcinoma will then imply not only an alveolar structure, but an epithelial origin also. The mode of genesis is the distinctive and definitive character; the alveolar structure is merely a result of contingent or non-essential factors.]

172. From the description we have given, it will be manifest that the

so-called cancer-cells are nothing other than proliferous epithelial cells; and we may therefore expect them to exhibit epithelial characteristics. Accordingly we find that they preserve throughout the traces of their descent. They are comparatively large, and have large vesicular nuclei containing nucleolar corpuscles; and they have certain habits of grouping peculiar to the parent structures. Cutaneous cancers (epitheliomata) contain cells exactly like those of the Malpighian layer, and they may undergo cornifying processes analogous to those which are normal in the case of the epidermis. Cancers starting in the intestinal mucous membrane are provided with cylindrical epithelium. But this maintenance of the ancestral cell-type has its limits.

When strings or wedges of epithelial cells penetrate the fibrous tissues, it invariably happens that the tightly packed elements affect each other mutually, and chiefly as regards their form (Fig. 65). We may see how this occurs by considering a section of one of these conical epithelial wedges—which from their appearance have been called **"bird's-nest bodies"** (concentric or epidermic globes). When the cells are isolated it is found that there are scarcely two alike in shape. This multiformity of the cells of cancer has long been a familiar fact; it has even been exalted into a characteristic feature. It obtains in squamous epithelioma and in cylindrical carcinoma, starting in the cylindrical epithelium of intestine or gland. The original type is only in a few cases preserved pure and unmodified.

FIG. 65.—Bird's-nest Body or "Concentric Globe" from an Epithelioma. × 250.

At the same time we must not look upon this multiformity as anything peculiar to cancer. Multiform cells may occur in other tumors—in the sarcomata, for instance. All we can say is—that in virtue of the peculiar mode of cell-multiplication in the carcinomata, multiform cells are especially apt to be produced in them. What is true of their alveolar structure is also true here. In consequence of their mode of development we always find that cancers are alveolar; but other tumors whose genesis is entirely different may nevertheless exhibit the same structure.

173. **Varieties of carcinoma** have been distinguished according to their site and place of origin, the form and texture of the cells, the arrangement of the cells, and the mode of epithelial infiltration dependent thereon, and finally the abundance and texture of the fibrous stroma. Many of these distinctions have now ceased to have any real significance. The title given to certain cancers of the skin or mucous membrane—namely, epithelioma or epithelial cancer—is now useful only as indicating conveniently their seat and histological structure. Formerly the title implied a contradistinction between cancer of the epithelia and can-

cer of the connective tissues. Other terms, like medullary, simple, or scirrhous, applied to various structural varieties of cancer chiefly originating in the glands, have also only a limited application ; inasmuch as an individual cancer may not have exactly the same structure throughout all its parts, or in all its successive stages.

Generally speaking, the form of the cancer depends on the structure of the matrix in which it is seated. A certain group of forms are found to recur perpetually in each particular organ. It would seem most natural *à priori* to divide the carcinomata into two groups—those, namely, which start in investing or surface epithelium, and those which start in glandular epithelium. Such a division might be preferable from a theoretical point of view ; but it is not always practicable, as it demands rather minute histological investigation. An epithelioma starting in a sebaceous gland has generally the very same appearance as one starting in a hair-follicle or in the epidermis. In cancer of the intestine, it would often be a matter of very great difficulty to decide whether the disease started in the simple lining epithelium, or in that of the crypts of Lieberkühn. For this reason it is advisable to classify the carcinomata under a few main types, distinguished by sufficiently well-marked anatomical differences. The following are the most important.

(1) **Squamous epithelial cancer.** The chief representative of this class is epithelioma or cutaneous cancroid (Fig. 62). This gives rise to warty and nodular tumors, or to diffuse thickenings of the skin. It is characterized by the occurrence in it of large epithelial nests, made up of large multiform squamous cells. Ulcers are very often formed by the breaking down of the new tissue.

If the section of an epithelioma be scraped, a gritty mass is obtained consisting mainly of nests and single cells. The nests often take the form of globes, in which the cells are arranged concentrically like the coats of an onion (Fig. 62, *i*). These at times become horny, forming what are called epithelial pearls. Epitheliomata in which these pearls are a distinct feature have been called horny or corneous cancroids. The tumor-cells of epithelioma are descendants of the superficial epidermis, and also of the epithelia of the hair-follicles and sebaceous glands. Squamous epithelial cancers occur in all the mucous membranes covered with squamous epithelium—in the mouth, pharynx, œsophagus, bladder, vagina, etc.

(2) **Cylindrical epithelial cancer.** This has its seat in mucous membrane, chiefly that of the intestine, but also in that of the uterus. It forms soft nodulated tumors which start in the columnar epithelium of the glands.

In consequence of active multiplication among the epithelial cells the glands become distended into more or less globular nests (Fig. 66). By mutual compression the cells assume very various forms, retaining their columnar character only at the periphery. Sometimes an unoccupied space or lumen remains at the centre. The cell-nests having thus the

appearance of gigantic gland-acini, the tumor has also been described as adenocarcinoma ; we reserve this term for the destructive adenoma described in Art. 169.

Glandular cancer of a like kind, with a coarse alveolar stroma, occurs in glands like the kidney and mamma, as well as in mucous membrane. In them it likewise starts in overgrowth and multiplication of the glandular epithelium. The difference between this variety and the last consists simply in the absence of tall columnar epithelial cells among the other constituents. This is due to the fact that the epithelium in which the growth originates is spheroidal rather than columnar.

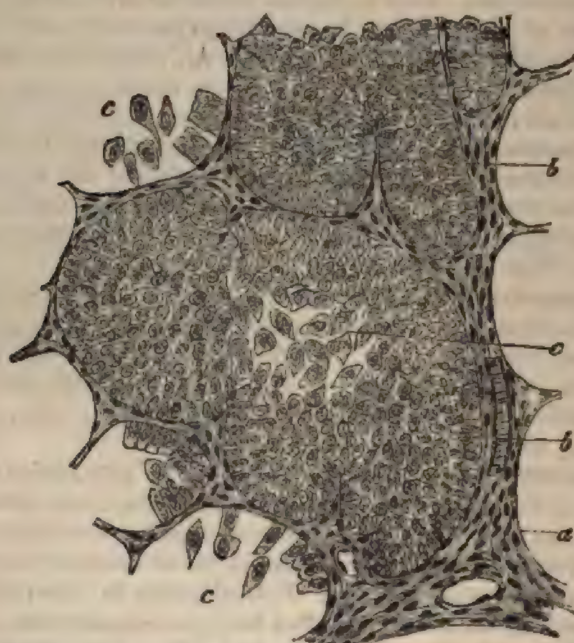

FIG. 66.—Glandular Cancer of the Uterus. × 250. (Hæmatoxylin staining.) *a*, stroma ; *b*, cancerous nests or loculi ; *c*, isolated cancer-cells.

(3) **Simple carcinoma** is a term often applied to a variety usually originating in glands, and forming rather firm nodulated tumors. In section these have generally a light grayish translucent look. The stroma and the cell-nests are often sharply distinguished from each other by the difference of their color ; especially when the cells have already undergone partial fatty change, and so look white or yellowish-white and opaque. By scraping the section we can often obtain a fairly abundant milky juice. The tumor has a somewhat coarse fibrous framework (Fig. 67, *a*), containing alveoli of various sizes and shapes filled with masses of epithelial cells. It particularly affects the mamma, and occurs also in the stomach, pancreas, and kidneys.

(4) **Medullary** (or encephaloid) **cancer.** When the cells are very abundant and the stroma delicate and scanty, the consistence of the tumor may become remarkably soft and semifluid. Such forms occur chiefly in mucous membrane, but also in the ovary, kidney, testis, etc. They are described as medullary or encephaloid cancers. They resemble very much the softer adenomata and sarcomata. An abundant milky cancer-juice may be expressed from the cut surface; it contains numerous cells and free nuclei, with fatty detritus and free oil-globules.

(5) **Scirrhus,** or scirrhous cancer. In this the cell-groups are small and scanty and the stroma coarse and dense. The tumor feels firm or even hard, and looks very much like a dense fibroma.

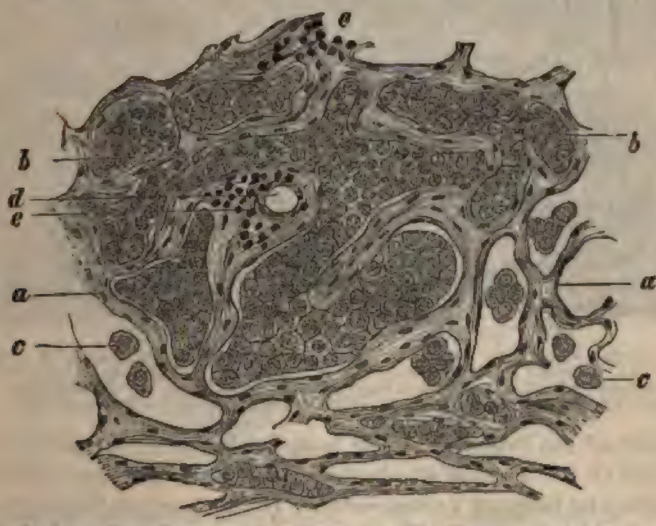

FIG. 67.—Section from a Simple Carcinoma of the Mamma. × 200. (Hæmatoxylin staining.) *a*, stroma; *b*, nests or loculi; *c*, single cancer-cells; *d*, blood-vessel; *e*, fibrous stroma infiltrated with small cells.

There is no sharp line to be drawn between scirrhus and simple cancer. Within one and the same growth we may find a part having the texture of scirrhus, and another resembling simple cancer (Fig. 68). The question is merely whether the stroma or the cellular elements predominate. The characteristic hardness of scirrhus is found at spots where the fibrous stroma is not so much alveolated as interspersed with small fusiform cell-nests (Fig. 68, *g*, *h*).

The cancer-cells often perish by fatty degeneration, and are then absorbed. The coarse fibrous stroma is left, looking like a deposit of firm scar-tissue. Cancers which have become hard and fibrous in this way are found not only in the mamma but also in the stomach, testis, ovary, and kidney.

(6) **Colloid** (otherwise gelatinous or alveolar) **cancer** occurs as a definite tumor or a diffuse infiltration. It is most frequently found in the alimentary tract and in the mamma, more rarely in the ovary or other or-

gan. It is characterized by the translucency of its substance. The stroma seems to contain masses of jelly rather than the usual more or less opaque cell-nests. The transparent glassy look may be apparent even on

FIG. 68.—Simple Cancer of the Mamma (Scirrhous in parts). (Magnified by means of a simple lens; same as Fig. 64.) *a*, nipple; *b*, mammary tissue; *c*, skin; *d*, galactophorous ducts; *e*, cancer-tissue replacing the gland-tissue; *f*, fat-lobules, normal or undergoing cancerous change; *g*, cancerous skin; *h*, cancerous infiltration of the nipple; *i*, normal acini; *k*, infiltration of fibrous tissue with round-cells.

the outside of the tumor. This is true, for instance, in the case of colloid cancer of the mucous membrane, which usually forms semitransparent papillary or fungous excrescences. In the mamma the colloid char-

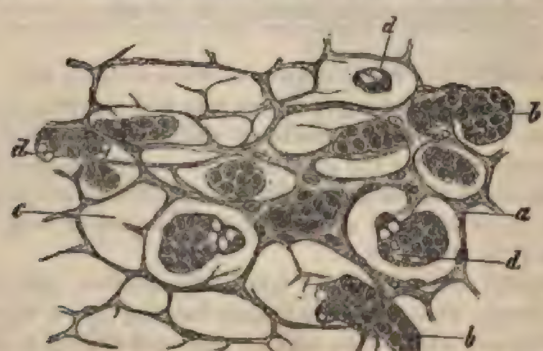

FIG. 69.—Colloid Cancer of the Mamma. × 250. (Hæmatoxylin staining.) *a*, stroma; *b*, cancerous cell-nests; *c*, empty alveoli; *d*, cells containing globules of colloid substance.

acter becomes apparent only on cutting through the tumor. It often happens that the whole tumor is not alike, some parts being translucent, others grayish or reddish like the more ordinary forms.

The colloid or gelatinous texture of the tumor is due to mucoid or colloid change affecting the cancer-cells (Fig. 69). It begins with the formation of clear globules in their interior (*d*). The cells then perish, and the globules coalesce with each other and with larger gelatinous lumps already formed. In this way a large homogeneous colloid mass is ultimately built up. It is not uncommon for all the cells over a wide area to perish in this manner, so that the stroma is the only formed constituent remaining. In other spots, cell-groups may still be found encircled by colloid masses (Fig. 69, *b*); in others again there is no colloid substance at all.

(7) **Carcinoma myxomatodes.** A cancerous tumor may likewise assume a gelatinous texture in consequence of mucoid change affecting the stroma (Fig. 70). With this metaplasia of the fibrous tissue there

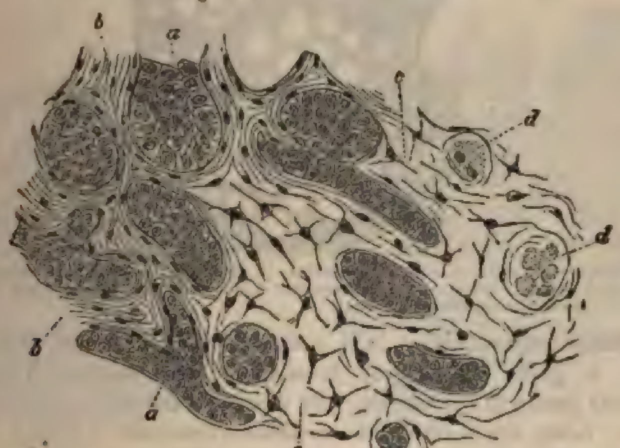

FIG. 70.—Carcinoma Myxomatodes of the Stomach. × 250. (Hæmatoxylin staining.) *a*, cancerous loculi; *b*, fibrous stroma; *c*, mucoid stroma; *d*, mucoid cancer-cells.

may also be associated a mucoid degeneration of the cancer-cells (Fig. 70, *d*); and this may increase considerably the transparent and gelatinous appearance of the growth. The connective tissue-cells of the stroma may also perish, so that we are often unable to find any traces of cell-structure over wide areas. The favorite seats of this variety are the same as those of colloid cancer.

(8) **Cylindroma carcinomatodes** is a very rare variety of cancer, characterized by the formation of homogeneous spherules within the cell-nests (Fig. 71).

These spherules, which are possibly to be regarded as masses of colloid substance, press asunder the other cells of the group (Fig. 71, *b*). If a considerable number of spherules form within the same loculus, the cells may be compressed into slender trabeculæ (*c*), and so come to form a kind of anastomosing network. This variety has been described as a cylindroma (Ziegler has only once met with it, and then in the lachrymal

gland). To distinguish it from the sarcomatous kind (Art. 163), it has been called carcinomatodes.

(9) **Giant-celled** (or myeloid) **cancer** is a form in which some of the cancer-cells attain an inordinate size. All parts of the cell—protoplasm, nucleus, and nucleolar corpuscles—contribute to this enlargement. They become at the same time remarkably transparent, and the general aspect is much as if the cell had imbibed a great quantity of water, and had in consequence swollen out enormously.

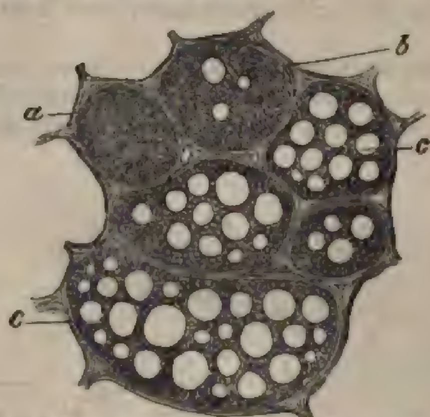

Fig. 71.—Section from a Cylindroma Carcinomatodes. × 150. (Carmine staining.) *a*, unaltered loculus or cell-nest; *b*, cell-nests with a few hyaline spherules; *c*, cell-nests reduced to a honeycombed reticulum by the formation of numerous hyaline spherules.

(10) **Melanocarcinoma** is a sufficiently distinct variety to deserve mention. It gives rise to gray, brown, or black tumors. The pigment is contained partly in the cancer-cells, partly in the stroma. It is seldom met with; being much rarer than melanotic sarcoma.

[References:—Waldeyer, "Virch. Arch.," vol. lv.; Rindfleisch, "Path. Histology," vol. i.; Lücke, Art. "Geschwülste" in "Hand. d. Chirurgie v. Pitha u. Billroth," ii.; Perls, "Allg. Path.," 1877; Paget, "Surg. Path.," Lectures 30 to 35; Lebert, "Des maladies cancéreuses," Paris, 1851.]

174. The **extension of a cancerous growth** is not at an end when the organ originally attacked is infiltrated throughout. Cancer pays small heed to the boundaries between the various tissues. Sooner or later (latest of all in encapsuled organs like the kidney), the cancerous process invades the neighboring tissues. Some of these, chiefly the specific tissues like glandular epithelium, muscle, bone, etc., disappear before the advancing growth. Fibrous tissue, on the other hand, is usually excited to proliferation, and new tissue and blood-vessels may thus be formed and converted into cancer stroma. Now and then other proliferations are set up in the neighborhood of the tumor, and in this way, for example, new bony growths may be formed.

In addition to this peculiar power of invasion, cancer has also in a high degree the power of originating **metastases** or **secondary growths.** The germs which give rise to these metastases are the cancerous epithelial cells, which are carried off to remote places by the blood or lymph. The first development of the secondary nodules starts in these, when they have found a suitable nidus. An epithelial germ may reach the liver, for instance, and become wedged in one of the terminal radicles of the vena portæ. If it finds adequate nutriment there, it begins to grow. It subdivides and multiplies, and thus a cell-nest is presently formed (Fig. 72) which distends the capillary vessel, and by compression causes the liver-cells to dwindle and atrophy. By the aid of the fibrous elements of the vessels, which proceed to multiply, and so furnish a fibrous stroma and accessory vessels, a secondary nodule is at length

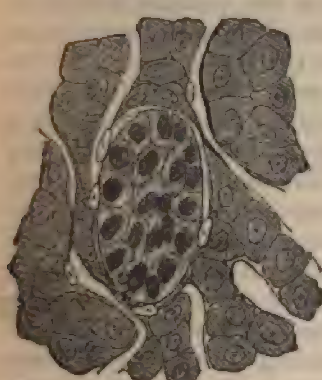

FIG. 72.

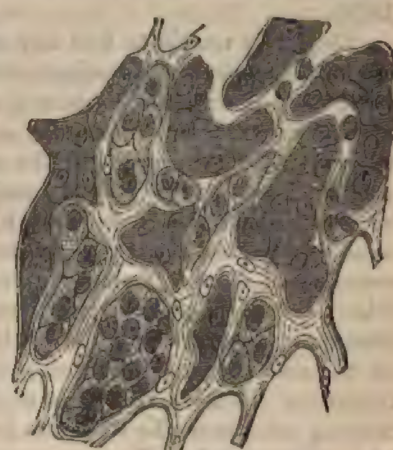

FIG. 73.

FIG. 72.—Section passing through a Cancerous Embolus of a Hepatic Capillary. × 300. (From a case of primary adenocarcinoma of the stomach; hæmatoxylin staining.) The cancer germs have just begun to develop into a secondary nodule.

FIG. 73.—Metastatic Development of Cancer in a Hepatic Capillary. × 250. (The primary focus was in the pancreas; fibrous tissue as well as cell-nests have been formed within the capillary.)

evolved, whose structure resembles in all points the structure of the parent nodule. The hepatic lobules are either pushed aside and compressed, or they are interpenetrated by strings of cancer-cells starting from the nodule. This is the result of the mode of growth of the nodule. It grows chiefly at its periphery, and extends along the open capillary channels (Fig. 73). In this way the capillaries themselves are one after another replaced by cancer-tissue. As this latter extends, the liver-cells gradually disappear.

The epithelial elements of the secondary nodules are to be regarded as, without exception, the progeny of the original cancer-cells transplanted from the parent growth. The fibrous tissue in which they are embedded is furnished by the connective-tissue elements of the blood-vessels.

[The origin of the cancer-cells in secondary nodules has been the subject of as much discussion as the genesis of the primary growth. Even now a certain amount of disagreement exists on the question. Rindfleisch, Klebs, Gussenbauer, Weil, and others, maintain that the connective-tissue cells, and especially the endothelia of the blood-vessels and lymphatics, take an active share in forming the cancer-cells of the metastatic growths. Gussenbauer ("Langenbeck's Arch. f. Chir.," xiv.) and Weil ("Wien. med. Jahrb.," 1873) go so far as to say that even striated and non-striated muscle-fibres may be stirred up (in a manner infected) so as to produce cancer-cells. Simon, Creighton, Moxon, and others in this country, have put forward like theories; they are accustomed to speak of a "spermatic" influence exerted by the transported germs upon the tissue-elements of their new seat ("Trans. Path. Soc.," 1874).

Ziegler is unable to find any satisfactory evidence for such a view. He made numerous investigations bearing on the question, and under his guidance Fronista examined a multitude of secondary growths in various organs; but no certain grounds for the theory were ever discovered. Active changes in the fixed cells were often very beautifully shown; but wherever it was possible to trace the fate of these cells it was found that they merely went to form the type of tissue which they would reproduce in normal circumstances. The osteoblasts of the periosteum and marrow form bone or fibrous tissue; endothelial cells likewise produce only connective tissue. It is not, however, to be inferred that these investigations absolutely and certainly exclude the possibility of a cancerous transformation of the products of connective-tissue proliferation. When a tissue has undergone extensive proliferous changes, nothing certain can be made out from it regarding the origin or the fate of individual cells. The cancerous embolus acts like a foreign body. Round it are set up inflammatory infiltration of leucocytes on the one hand, and multiplication of the fixed cells on the other. Both processes result in fibrous hyperplasia, which in many cases goes to form a new stroma for the growing nodule. The same processes are thus repeated here as occur in the fibrous structures of the primary focus. It is therefore well to hold by the doctrine of Remak and Goodsir—at least until it is certainly disproved—that as the descendants of the different embryonic layers are never transformed into each other in normal circumstances, so also under pathological conditions no such metaplasia can occur. Even the transformation of one epithelial formation into another suggested by some (Rindfleisch, "Path. Histology," Art. 531; Perls, "Virch. Arch.," vol. lvi., etc.) has not been established. When carcinomata of the liver are examined the liver-cells are seen to dwindle and perish, but not to change to cancer-cells. Even in cases where mammary cancer penetrates the corium and reaches the epithelial layers of the skin, it is always possible to distinguish clearly between the cancer-cells and the true cutaneous epithelium.]

175. Carcinoma is very prone to undergo retrogressive change. In the juice scraped from the cut surface of a cancer we may nearly always find cells which are fatty or disintegrating. This is especially the case in soft quickly growing tumors. If the fatty change is extensive the affected spots look white and opaque, and by and by break down into a creamy pulp. The disintegrated cells may also become condensed into cheesy masses. More commonly, however, we find that a part of the cells become absorbed. In tumors lying beneath the surface of an organ or raised above its general level, a central depression or dimple may thus be formed. The tumor is then said to be **umbilicated.** In cancers with a dense stroma, in which the disappearance of the cells is accompanied by hyperplasia of the fibrous elements, we may find the original growth replaced by a dense coarse deposit of fibrous tissue containing few, if any, cancerous cell-nests. This transformation is specially frequent in the case of mammary and gastric scirrhus.

Mucoid degeneration has already been discussed (Art. 173). Amyloid degeneration of the stroma has frequently been observed.

The necrotic disintegration of cancerous growths, and the consequent formation of **cancerous ulcers,** deserve special mention. Tumors of great size may in this way be wholly destroyed. In intestinal cancer, for example, it is no rare thing to find after a certain time nothing but an ulceration, replacing the original tumor, and bearing hardly any resemblance to it. If the ulcerative process is not far advanced, the remains of the tumor may be recognized as nodules or papillary excrescences rising from the base or border of the ulcer. In later stages the base may be smooth and clean, consisting simply of firm fibrous tissue; while the edges rise like ramparts, or are beset with papillary or nodular growths. Now and then these may disappear in like manner, and the ulcer appears as a non-cancerous sore with an indurated base. Even on section it may not always be possible with the unaided eye to decide whether the tissue still contains cell-nests or not. We must in such cases have recourse to the microscope.

Cutaneous or epitheliomatous cancers, like those of mucous membrane, may also ulcerate; and so, too, may cancers of the mamma or other subcutaneous glands. The surface of these breaks down, and great putrid or fetid ulcers are the result.

The seat of an ulcer is always the seat of a more or less intense inflammatory infiltration. Sometimes this results in vigorous granulative proliferation, the granulations rising above the surface as fungous excrescences. They are distinguished from ordinary granulations by the cell-nests they contain. From this granulation-tissue ordinary cicatricial tissue may be elaborated. A sort of local healing and recovery may thus result—from the destruction of the tumor, and the formation of granulative and cicatricial tissue. The growth may seem to have altogether disappeared. But this healing is only local and relative, and it does not last. Microscopic examination shows that the cancerous invasion of the

deeper structures still persists. The formation of secondary growths, even after the surface ulceration is scarred over, testifies to the fact that the malignancy of the process is not removed with the removal of the primary growth.

176. Adenoma and carcinoma may be combined with other neoplastic formations; that is to say, the stroma may be composed of other than fibrous tissue. In the first place, it must be remembered—that as cancer invades successive tissues, the most various structures may in turn be utilized to form its stroma. Thus when a uterine cancer reaches the muscular coats of the organ, we find that the stroma of the tumor contains smooth muscular fibres. When secondary nodules form in the liver, we often see liver-cells, atrophied no doubt but still recognizable, in the trabeculæ of the stroma. The new-formed tissues which actually originate in the stroma are to be distinguished from such pre-existing formations. In the former case we may find that not only fibrous tissue but even cartilage or sarcomatous tissue has been developed. Such neoplasms are described as complex or **mixed tumors.** They are most common in the testis and parotid gland. They resemble the simple carcinomata in their general relations.

Fatty degeneration
Caseous "
Fibrous p. 462.
Mucoid
Necrosis
Ulceration
[illegible]

CHAPTER XXVIII.

ETIOLOGY OF TUMORS.

177. Our knowledge of the etiology of tumors is still very defective. What we have to say on the subject is, generally speaking, largely hypothetical.

We might at first be inclined to regard a tumor as the result of a local overgrowth of tissue, and to look for the conditions of its development among those which determine ordinary hyperplasia. But facts soon appear which tend to show that the processes are not parallel. There is, first, the histological diversity of the tumor (Art. 136) from the matrix in which it grows. Secondly, there is the associated impairment or extinction of the physiological function of the matrix-tissue. These facts do not suggest a mere over-active growth *in situ*. The anatomical facts are thus against our regarding tumors as localized hyperplasias. It follows that we cannot expect to discover the efficient causes of tumor-growth among the factors which give rise to such hyperplasias.

Nor can we fairly compare the tumors with the inflammatory new-formations. Tumors may indeed contain foci which are infiltrated with leucocytes. But these are of secondary significance. The entire process of neoplastic histogenesis shows that it is something quite different from the formative processes which originate in inflammation. We thus exclude at once the possibility of attributing the growth of a tumor to a traumatic lesion, at least in any immediate or direct way. Clinical experience bears this out; for, if now and then we have tumors developed in a substratum of tissue which has been injured and has undergone inflammatory change, it is on the whole a rare occurrence, and does not prove that such injury would of itself suffice to set up tumor-formation in previously healthy tissue.

This being the case, we are perforce constrained to admit that other factors must be sought, if we are to explain the genesis of tumors.

If we did not know that tumors may develop at the most various periods of life—nay, that many forms are wont to appear only in advanced age, it might perhaps suggest itself to look for their etiological factors in the embryo—to regard them, in fact, as local malformations. But the peculiar modes of occurrence referred to, and the observation that tumors originate in tissues which before looked perfectly normal,

would scarcely make us regard such an embryonic theory as very probable beforehand.

Cohnheim has very recently propounded an **embryonic hypothesis** of another kind. We are not to refer the actual development of the tumor itself to the embryonic period, but are to attribute its appearance in later life to the persistence of germinal embryonic tissues in the otherwise mature organism (Cohnheim, "Allg. Path.," i.). A tumor takes its rise in what we might call a belated rudiment—a focus of formative embryonic tissue, which has not been utilized in elaborating the normal tissue of the part—and so has lingered on unchanged. Cohnheim therefore defines a tumor as—an atypical new-formation starting in a latent embryonic rudiment. The tumor-germs, consisting as they do of embryonic cells, may be very small and so elude observation. It is even conceivable, he thinks, that the germinal cells may be quite unrecognizable among the ordinary physiological elements of the part. They may linger on for a long time inactive. It is only when they are favored by the external conditions—such as the supply of nutriment, and their relation to the surrounding tissues—that they begin to multiply and to form a tumor. In this way it becomes possible that a traumatic lesion may set up the active change. In most cases, however, the awakening impulse is beyond our power to discover.

We cannot deny that Cohnheim's hypothesis would explain satisfactorily many of the peculiarities of tumors. Those growths, for example, whose structure reminds us so strongly of earlier developmental stages of particular tissues, would be acquitted of their (at present) unaccountable heterology. It also tells in favor of the theory—that a class of tumors does actually exist, of which we can say with certainty that they date their origin from the embryonic stage. At the same time we may well question whether our knowledge of the subject justifies us in attributing an embryonic origin to all tumors, or whether we should accept the theory only with considerable limitations.

[Cohnheim bases his view mainly on the arguments—that many tumors have been shown to be hereditary; that many exist at birth, or at least develop in infancy; that they show a preference for sites where in earlier developmental stages some complication of structure occurred, *e.g.*, for the places where diverse epithelial formations pass one into the other (lips, anus, stomach, cervix uteri), or for parts where the entire process of development is highly complex (genital apparatus). Finally, he holds that the atypical structure of tumors generally is in favor of his account of them.

It must be granted that these arguments speak strongly for the hypothesis. They at least make it highly probable for certain classes of tumors. But they do not suffice to prove its applicability to all.

The view that tumors arise in consequence of injury, especially of frequently repeated irritation, is very widely accepted (Virchow "Die

krankhaften Geschwülste;" Krönlein, "Lang. Arch. f. klin. Chir.," xxi.; Kocher, Art. "Krankheiten des Hodens," "Handb. d. spec. Chir. v. Pitha u. Billroth;" Bögehold, "Virch. Arch.," vol. lxxxviii.). Cohnheim has justly objected to this view—that the number of cases of tumors in which antecedent injury has been demonstrated does not reach more than fourteen per cent. of the whole number, and is by some given as seven per cent. (Boll, "Das Princip des Wachsthums," Berlin, 1876; S. Wolff, "Zur Entstehung von Geschwülsten nach traum. Einwirk.," In. Diss., Berlin, 1874; Von Winiwarter, "Beiträge z. Statistik d. Carcinome," Stuttgart, 1878). From this we may infer that an injury may perhaps give rise to a tumor; but that neither injury nor inflammation is at all a necessary antecedent.]

178. We are acquainted with a considerable number of forms of **congenital tumor** whose origin can be referred with more or less certainty to the embryonic period. Of these it is, however, to be remarked—that their structure and composition are only in part analogous to those of the post-embryonic growths hitherto discussed. Many of them possess a structure entirely peculiar to themselves, so that they cannot be classed with any of the preceding tumors. They are therefore regarded by all authorities as special and peculiar formations, and are distinguished as teratomata.

Teratomata, or teratoid tumors (Art. 13), are congenital growths, which are remarkable for the heterogeneity of their constituent elements. They may be large even at birth, or they may grow from small beginnings to a large size after birth. They may contain fibrous tissue, cartilage, bone, muscle, skin, hair, nerves, gland-tissue, and simple cellular or embryonic tissue. At times they may have the look of complex histioid tumors; but the combinations they present are usually much more various and heterogeneous than in any ordinary histioid growth. We even meet in them with structures which recall the appearance of some normal organ—the differences lying chiefly in the rudimentary nature of the outward shape or configuration, and the abnormal site. Sometimes the various tissues are grouped into something like orderly disposition, giving one the impression of a more or less organized fœtus.

Teratomata, when externally visible, are usually placed at parts of the trunk corresponding to those at which double monstrosities cohere. These are chiefly the lower end of the spine, the head, and the neck. Internal teratomata are usually connected with the genital apparatus.

Such teratomata are some of them true double monstrosities. One fœtus has been surrounded and enclosed by another, and so has become stunted and ill-developed (Art. 13). The remainder are due to some misdevelopment of the tissues within a single fœtus.

Dermoid cysts form a special class of teratomata. They are cysts whose inner surface has the same structure as the normal skin; but they occur in places where no skin is ever found normally. Their commonest

seat is in the generative organs, especially in the ovary. More rarely they are found in other parts, such as the peritoneum, neck, and around the orbit. The smallest examples form little cysts which, as in the ovary, are distinguishable from their contents. The contents are usually greasy, semi-solid, yellowish-white, and interspersed with hairs. The wall is thicker, firmer, and whiter, than that of the Graafian follicles. Under the microscope it is seen to be composed of a corium and epidermis; it may even contain hair-follicles and sebaceous glands, or more rarely, sweat-glands. Now and then an adipose layer, like the subcutaneous fat, is found beneath the corium. In rare cases, flat or irregular fragments of bone or cartilage, and even teeth, are found beneath the cutaneous layer. The teeth may also be found free within the cyst. Very rarely the cyst-wall contains muscular or nervous tissue. The larger dermoids, *i.e.*, those reaching from the size of a walnut to that of the fist, are sharply marked off from the surrounding tissues by a fibrous capsule. They enclose large quantities of oily or greasy detritus, interspersed with fair or reddish hairs.

Dermoids are found in young individuals as well as old. Some are found even in the new-born. They grow very slowly. Judging by the special character of their lining membrane, these formations would seem to be derived from the same rudimentary elements as the external skin. They are probably due to aberrant germinal cutaneous cells from the epiblast, which have somehow wandered to an abnormal site, and there have at a later stage begun to develop after their kind.

[References on the subject of teratomata and dermoid cysts:—Art. 13; Kohlrausch, "Müller's Arch.," 1843; Lebert, "Gaz. méd. de Paris," 1852; Remak, "Deutsche Klinik," 16, 1856; Heschl, "Prager Viertelj.," 1860; Lücke, "Handb. d. Chir. v. Pitha u. Billroth," ii.; Haffter, "Arch. d. Heilk.," xvi., 1875; Panum, "Virch. Arch.," vol. lxxii.; Klebs, "Handb. d. path. Anat.;" Danzel and Martini, "Arch. f. klin. Chir.," xvii.; Waldeyer, "Arch. f. Gynäk.," i.; Wilson Fox, *Journal of Anatomy*, 1865; Gordon, "Med.-Chir. Trans.," xiii.; Paget, "Surg. Path.," Lecture 23.]

179. Besides the teratomata there are other tumors more nearly allied in structure to the ordinary forms, which are either congenital or appear so soon after birth that their origin may, with more or less certainty, be referred to the embryonic period. The best-known examples are the **congenital angiomata** and **pigment-spots** (beauty-spots, moles) in the skin. The former have already been discussed (Arts. 148-150). Of the latter we have merely to say, that they appear as brown or black slightly raised patches in the skin, and are composed of tissue exactly resembling alveolar sarcoma (Fig. 54) covered over with epidermis.

We may likewise mention in this connection—certain cutaneous fibromata; enchondromata of the skull, spinal column, and fingers; myxo-

mata of the jaws ; renal adenomata and cancers ; and cystic adenomata seated on the sacrum and communicating with the central canal of the spinal cord.

The number of really congenital tumors observed is by no means great. Cases of tumors appearing in the earlier years of infancy and referable to embryonic conditions are more numerous. Of this kind are the sarcomata of infancy ; especially the form of myosarcoma of the kidney referred to in Art. 153. It is not impossible that some of the ovarian adenomata may date back to the embryonic period. If we consider carefully the scanty details we possess of congenital tumors, taken in conjunction with the familiar facts of post-embryonic tumor-formation, we must admit that the support which Cohnheim's theory derives from this side of the subject is not very great.

It must not, however, be forgotten that this theory requires the existence, not of congenital tumors, but only of congenital rudiments of tumors. As to these latter our knowledge is unfortunately very small. It is almost entirely confined to the pigmentary and vascular nævi we have mentioned. They may be regarded, and with equal justice, either as germinal rudiments of tumors, or as developed growths. The former view is justified by the fact that in later life it is not uncommon for these structures to develop into true malignant tumors.

Tumor-germs in bone were discovered some years ago by Virchow ("Berlin. acad. Monatsbericht," 1875). He showed that islands of cartilage, which remain untransformed in the general ossifying process, may in later life become the starting-points for the formation of chondromata.

Nothing certain is known of embryonic epithelial germs, such as may subsequently develop into tumors. Their existence may be surmised in the case of early epithelial tumors of the ovary, kidney, or intestine ; but it has not been demonstrated. The frequently observed accessory glands occurring in connection with the pancreas, mamma, thyroid, etc., are not to be regarded as mere germinal rudiments, inasmuch as they contain fully developed gland-tissue.

From what we have said, then, it will be seen that the histological evidence for the existence of embryonic germinal tissue in the fully developed organism is very slender.

[Ziegler describes a tumor of some interest which he found in the small intestine, seated in the *submucosa ;* it was as large as a pea, and was made up of minute cysts. It should probably be regarded as a local misformation, rather than a deposit of germinal tissue. Its cysts contained papillary excrescences covered with columnar epithelium ; and small gland-tubules were found in the cyst-walls. It is conceivable that, from a misformation of this kind, a true tumor might at some time or other begin to develop.

References on congenital tumors : — Virchow, "Die krankheit. Geschwülste ;" Duzan, "Du cancer chez les enfants," Paris, 1876 ; Ahlfeld,

"Arch. f. Gynäk.," xvi. ; Rohrer, "Das primäre Nierencarcinom," Zürich, 1874 ; Maas, "Berl. klin. Woch.," xlvii., 1880 ; C. Vogt, "Ueber angeb. Lipome," In. Diss., Berlin, 1876 ; Chiari, "Jahrb. d. Kinderheilk.," xiv. ; Weigert, "Virch. Arch.," vol. lxvii. (renal adenoma).

Many authorities are of opinion that Cohnheim's theory is strongly borne out by the experiments of Zahn ("Sur le sort des tissus emplantés dans l'organisme," International Medical Congress, Geneva, 1873), and Leopold ("Virch. Arch.," vol. lxxxv.). They took bits of cartilage from a living fœtal rabbit, and transplanted them into the peritoneal cavity and anterior chamber of the eye of an adult rabbit. The cartilage continued to grow, while pieces of cartilage taken from animals after birth were merely absorbed. This scarcely seems sufficient ground for Cohnheim's generalization. The faculty of growing after transplantation is not manifested by all fœtal tissues ; many or most of them are dissolved and absorbed by the disintegrating action of the fixed and migratory cells of the new matrix (Leopold, "Arch. f. Gynäk.," xviii.). These experiments only show that fœtal cartilage has the power of persisting, and even of growing for a time, in spite of defective nutrition, and the absorbent action of the cells of the other tissues.]

180. The inadequacy of the evidence for the existence of germinal embryonic rudiments in the adult tissues makes it appear a somewhat bold step to ascribe an embryonic origin to all tumors whatsoever. The observed and recorded cases do not justify us in saying more than that some tumors arise in rudimental structures, which were histologically distinguishable from the normal tissues before the tumor began to grow. And even in saying so much we must not interpret the term embryonic too literally. Embryonic formations are such as possess a structure resembling that of undeveloped tissue—an indefinite structure preceding the definitive or specialized structure. Tissues that are merely misdeveloped, pieces of tissue (such as epithelium or gland-tissue) displaced from their proper seat and transplanted elsewhere, as in the case of accessory glands and dermoid cysts, are not what we understand by embryonic tissues.

The class of tumors referable to embryonic rudiments will be somewhat enlarged, if we enlarge the signification of the term embryonic so as to include under it all tissues in process of active and energetic growth.

So long as an organ continues to grow, so long are multitudes of new cells formed in it. These formative cells may be called embryonic, inasmuch as they continue to multiply actively, and so are nearer akin to the cells of the embryo than to those of mature tissue. In this way osteoblasts and osteoclasts and the proliferating cartilage of growing bone, the cells of the enlarging uterus in pregnancy, the tissue of the mamma preparing for lactation, all might be described as embryonic. If the hypothesis be thus extended, a whole series of tumors will certainly be com-

prehended under it. When, for instance, a tumor develops in the mamma or uterus in connection with parturition, or a sarcoma or enchondroma forms in bone, periosteum, or marrow during ossification, it is not difficult to believe that the same cells which are building up the normal tissue may also give rise to the tumor.

But if we extend the meaning of the term embryonic so as to include all this, where are we to stop? Growth, *i.e.*, restoration and replacement of what is being used up, continues throughout life. Surface epithelium is cast off and is regenerated; glandular epithelium is used up and replaced; even bone, though it seems so stationary, is exposed to changes at all stages of life—it is being resorbed by the osteoclasts and built up again by the osteoblasts.

If all post-embryonic processes of growth are to be styled embryonic, we cannot refuse to give the same title to all the processes of new cell-formation that occur during life. If this be granted, embryonic tissue becomes exactly the same as that which Virchow called proliferous tissue, *i.e.*, tissue capable of proliferation. We gain nothing by the mere substitution of one name for another; in the present case we lose something, for we are no longer able to distinguish in expression between embryonic and post-embryonic formation. For this reason it is better to confine the term embryonic to tissues which actually originate in the embryonic period.

[The fact that we really know nothing of the persistence of true embryonic tissue—or, in other words, that it has not been histologically demonstrated—is acknowledged by Cohnheim. He seeks to explain the fact by supposing that the embryonic foci are very small and hard to distinguish; or even that the germinal cells may be mingled with the normal elements and so not distinguishable at all. It is not easy to imagine how embryonic cellular germs can possibly remain unchanged in the midst of mature tissue. Cohnheim and Mass ("Virch. Arch.," vol. lxx.) have shown that living tissue, such as periosteum, when introduced into another tissue like the lung, may continue to grow for a time; but afterward it is absorbed and destroyed by the tissue in which it lies. An embryonic germ seems to have but three courses open to it. It may remain embryonic; in this case it is as it were alien to the tissue in which it lies, and will be absorbed like an organic foreign substance. It may assimilate itself physiologically as well as anatomically with the surrounding tissue, taking part in its physiological function and working with it; in this case it loses its embryonic character. Or thirdly, it may develop into an independent formation, interpolated as it were into the general system; in this case it forms what we call a congenital tumor (nævus, adenoma, sarcoma).

Hasse has attempted to give Cohnheim's hypothesis a morphological basis ("Die Beziehungen der Morphologie zur Heilkunde," Leipzig, 1880). The morphologist distinguishes two kinds of substances within

the organism: one kind undergoes a series of transformations, the other provides for the formation of new tissue. The latter he describes as "embryonic substance." It is represented by cells which have undergone little or no transformation, and are the more apt to multiply the less their original character and structure has been modified—the nearer they stand to the formative cells of the embryo. From these cells only can new tissue be formed. Tumors are especially likely to be developed at spots where these "embryonic cells" are abundant and unmodified. Hasse's distinction between proliferous and non-proliferous tissue-elements is perfectly just (Arts. 84–89); and any one may if he chooses call the former embryonic (as do French writers especially). In this case, however, the antithesis, on which Cohnheim lays so much stress, between the cells of the embryo and the proliferous elements of the organism after birth, simply ceases to exist.]

181. It is plain, from the above, that we do not think the hypothesis tenable which refers all tumors whatsoever to pre-existing embryonic germs. Anatomical investigation forces us rather to the conclusion that tumors may arise in tissues that are in very different states—embryonic, growing, mature, or retrogressive.

What is then the efficient cause of the formation of a tumor? It is as yet impossible to give any precise answer to this question. It is highly probable that the causation of the various classes of tumors is not subject to one law only, but to several.

The entire behavior, anatomical and biological, of tumors justifies us in regarding them as formations more or less emancipated from the matrix-tissue. It is true they draw their nutriment from the organism, and cannot continue to grow without its support. In other respects, however, they behave like independent growths isolated from the rest of the organism. It is in this independence or quasi-isolation that the etiological difficulty really lies. How does the neoplasm thus assume properties distinct from those of its surroundings? We believe that the phenomenon is ultimately due to some change affecting individual elements of a tissue, whereby they are rendered dissimilar to their neighbors. The change is manifested especially in this—that the normal checks to the indefinite growth of the proliferous cells (Arts. 78–83) are inoperative or inadequate; either because the formative and productive energy is increased, or because the restraining influence of the surrounding structures is diminished, or from both causes together.

In the case of tumors appearing in the organism during the stage of development, it is most natural to suppose that the originating cause lies in an increased local growth due to intrinsic conditions; or, it may be, in a disturbance and diversion of the developmental process from its normal course. What the ultimate factors determining these deviations may be we know as little as we do the causes of gigantic overgrowth or local dwarfing of a limb or organ. When the anatomical and physiologi-

cal relations of the affected tissue are altered to a certain extent by this local change, it would seem as if the tissue had no longer the power to maintain the normal direction in which its development should proceed. The altered relations (such as misplacement, etc.) seem to involve the withdrawal of the limiting and directing influence exerted on the growing tissue by its environing structures. The result is the development of a tissue of abnormal type, a local misformation in the histological as well as the anatomical sense. The tumors whose genesis is probably of this kind are chiefly the connective-tissue growths of childhood. Among epithelial tumors we may also perhaps include the few observed cases of renal and intestinal cancer, and of ovarian adenoma, in infants.

It is thus not impossible that tumors of the developmental period may arise from causes similar to those which give rise to local malformations in the stricter sense of the term. Arrest of the process by which osteoblastic cells are transformed into bone might thus, for example, give rise to an abnormal formation of tissue such as cartilage, in other words, to enchondroma ; or, by encouraging an over-abundant cellular growth, to sarcoma.

Tumors arising in a mature tissue are to be explained only by supposing some antecedent alteration over a more or less extensive region of the tissue. This alteration must be of such a kind as to favor the emancipation of the subsequent neoplasm from its matrix-tissue, without at the same time diminishing the neoplasm's own productive power. This last, indeed, must rather be increased. In this way we may perhaps explain the operation of a traumatic lesion in inducing the growth of a tumor. In special circumstances it is conceivable that such a lesion may fulfil both the essential conditions we have named.

In the case of the connective-tissue growths of later life, it would seem as if increased cell-activity were always a necessary condition for their development. This must presumably always be a condition of tumor-formation in tissues whose cells are replaced but slowly or not at all. The primary impulse which excites the cells to active growth may be derived from some change either in the cells themselves, or in the intercellular basis-substance.

With regard to epithelial tumors, anatomical investigation shows that increased cell-production is not an indispensable prerequisite. In the carcinomata of later life, for instance, it would appear that the origin of the neoplastic growth is to be looked for, not so much in any increased activity on the part of the cells, as in a change of mutual relation between the several constituents of the tissue. Thiersch has pointed out—that in old age this latter effect may be due to certain retrogressive changes which then make their appearance. In the corium, for instance, such changes lead to a loosening of its texture, and so modify the relations of the epithelial cells to the fibrous tissue. This modification may make itself felt in one of two directions. In the first place, the epithelium, always in process of decay and replacement, may

in the course of its physiological growth and multiplication penetrate to regions which are normally devoid of epithelium. Loosening and displacement affecting the fibrous basis of an organ may give rise to something like fissures or spaces with free surfaces, and into these the contiguous epithelium may readily penetrate and grow. The first sproutings or outgrowths of glandular or lining epithelium may conceivably take place in this manner. We might fairly expect that the fibrous structures would, as it were, rise up against the intruder, and attempt to eliminate it as a foreign substance. This may well happen in many cases, and then the further advance of the process will be checked. In other cases it does not happen, probably because the invaded tissue is no longer in its normal or healthy state. We have, indeed, evidence of vascular alteration, infiltration of leucocytes, and even of new-formation of vessels and fibrous tissue ; but this, the normal eliminating process, is feeble and sluggish, and is inadequate to deal with the intrusive epithelium. The vascular changes and the increased afflux of nutriment tend rather to react favorably upon the epithelium, and to foster its reproduction. It becomes gradually more and more active—and so the foundation of a carcinoma is laid.

It seems not improbable that the process of neoplastic development does in fact occasionally pursue this general course. In other instances, it may well be that the fibrous basis-substance has a certain intrinsic predisposition favoring the formation of cancer, while the primary impulse which brings this into play is afforded only by some increase of formative activity on the part of the epithelial cells.

[The instructive discussion on the nature of cancer reported in the "Trans. Path. Soc.," 1874, should be consulted in this connection. For an exposition of the constitutional theory, which makes cancer a specific blood disease, see Paget, "Surg. Path.," Lectures 34, 35. See also Paget and Moore, "Holmes's Syst. of Surg.," vol. i.; Wilks, "Guy's Hosp. Rep.," 1872.]

SECTION VII.

PARASITES.

CHAPTER XXIX.

GENERAL CONSIDERATIONS.

182. A **parasite** is a living organism inhabiting another living organism, and deriving its nutriment either from the tissues or from the food-supply of its host. The parasites inhabiting man are some of them animal, and some of them vegetable. If they inhabit the superficial parts of the skin or mucous membrane they are called **ectozoa** (or epizoa), if animal, and **epiphytes**, if vegetable; if they inhabit the deeper structures they are **entozoa** and **entophytes**, respectively. The parasitic animals occurring in man belong to the classes of Arthropoda, Scolecida (embracing the Platyelminthes and Nematoidea), and Protozoa. The vegetable parasites are all of them Fungi, and belong to the subdivisions Schizomycetes (bacteria), Blastomycetes (yeasts), and Hyphomycetes (moulds).

The various parasites are of very various importance. Many of them produce no perceptible injury to the tissue in which they lie. Others produce very serious local changes, but have no power to extend their influence to remote tissues. Others invade the system, so to speak, and migrating in various directions produce multiple local affections. Many are conveyed throughout the body by the blood or lymph, in which case serious general affections and frequently death itself are the result. The great majority of parasites, and especially the vegetable parasites, increase and multiply within the body, often to an enormous extent. Others, chiefly the animal forms, pass only a part of their existence within the body. The local changes they produce are generally confined to the mechanical compression and destruction of tissue, and to the setting up of inflammation. They affect the system as a whole by abstracting nutriment and oxygen from it, and by giving rise to multitudes of centres of disturbance; while many of them generate actual poisons. The Schizomycetes or Bacteria play the most important part of all. It is they of all the parasites that have most power of exciting general or systemic affections. The Blastomycetes and Hyphomycetes, fungi akin to the yeast-fungus and mould-fungus respectively, exert a merely local influence. The animal parasites become dangerous in virtue of their size or multitude, or by penetrating into vital organs.

[Parasitism is an extremely common mode of life throughout the organized world. Innumerable plants and animals are parasitic either for a season or for the whole course of their life. Accordingly there are few living organisms that are not inhabited by parasites. A plant or animal which merely inhabits the body of an organism is not necessarily a parasite. The term is only applicable to organisms nourished at the expense of their host.]

CHAPTER XXX.

THE SCHIZOMYCETES OR BACTERIA.

Morphology, Development, and Classification.

183. The Schizomycetes or Schistomycetes, frequently included under the general term **Bacteria,** belong to the Protophytes—the smallest and simplest of all plants. Many of them are so small that they approach the limit of visibility, even when the highest powers of the microscope are used. When they occur in animal tissues they are to be distinguished only with great difficulty, and by special methods. Special reagents or staining processes must be employed ; sometimes certainty is only reached by experimental cultivation of the products of disintegration of the tissue in question. That they do occur in animal tissues is now established beyond all doubt. Their growth and multiplication have been experimentally demonstrated.

The Bacteria are all of them unicellular organisms devoid of chlorophyll ; they are often, however, aggregated into larger or smaller colonies. Cohn has classified them according to their form into **Spherobacteria** (globular cells), **Microbacteria** (minute rod-like cells, Bacteria proper), **Desmobacteria** (larger rod-like or filiform cells, Filobacteria), and **Spirobacteria** (twisted or spiral cells). Movements are noticed in the three latter forms ; their protoplasm is therefore contractile. Neither potash, ammonia, nor dilute acids destroy them, so it is probable that they possess a bounding membrane. Bacteria grow longitudinally ; new cells are formed by transverse subdivision. These remain in connection with each other, or become detached.

Von Nencki's researches ("Journ. f. prakt. Chem.," 1879, "Beiträge zur Biologie der Spaltpilze," 1880) go to show that the Bacteria are composed of a peculiar albuminoid body which he has called mycoprotein. They contain only the minutest quantities of bodies resembling cellulose.

[The above classification of the Bacteria is taken from Cohn ("Beiträge zur Biologie der Pflanzen," vol. i. ; *Quarterly Journal of Microscopic Science*, 77, 79, 1873), and his work has been mainly followed in the next four paragraphs. He makes the following remarks on the general question of classification :—"I have come to the conclusion that the Bac-

teria are as capable of exact specific classification as other plants. They lie at the limit of microscopic visibility. In the minuter forms it is therefore impossible to make out either structure or organization. The size and shape of the cells, and the mode in which they are combined into colonies, are then the only *differentiæ*; of these, however, it is not always easy to say whether they indicate original specific distinctions, or whether they depend on external conditions and lie within the limits of variability of one and the same species. Size is the easiest feature on which distinctions may be based, though even this is by no means easy to determine in the minuter forms. Differences in the mode of reproduction are only discoverable in the higher forms, such as the Bacilli. The genera of Bacteria have not the same significance as those of the higher plants. They are based chiefly on the characters of the vegetative cell-forms, not on the reproductive features. Every form distinguished by prominent or obvious characters is provisionally furnished with a generic name; smaller deviations serve to designate the species. It is thus not at all impossible that some of such species and genera may really represent different developmental stages of one and the same fungus." Since this utterance of Cohn's a great number of researches have been made into the growth and multiplication of the Bacteria. Koch especially has devoted himself to the subject ("Mittheil. a. d. kaiserl. Gesundheitsamte," Berlin, 1881). After long-continued experiments on cultivation, in which bacteria were bred in nutritive gelatine ("the dry process") he has reached the conclusion—that each species of bacteria possesses characteristic and easily recognizable peculiarities in respect of structure, form, size, and mode of growth of its colonies on the gelatine.

The Schizomycetes have been very variously named by different authors. Pasteur speaks of them as *végétaux cryptogames ou microscopiques*, *animalcules*, *champignons*, *infusoires*, *torulacées*, *bactéries*, *vibrioniens*, *monades*, *mycoderma*. In Germany the terms *Monaden*, *Vibrionen*, *Mikrozyma* and (by Klebs) *Mikrospora* and *Monadine* have been used. Billroth introduced the term *Coccobacteria*. In England we have corresponding terms, with others like *monads*, *zymes*, *microzymes* (Sanderson), *microphytes*, etc.]

184. The **Spherobacteria** are the smallest of all bacteria. Under the microscope they appear as bright round or ovoid spherules of scarcely measurable size. Two genera are distinguished: *Micrococcus* (Fig. 74, **1**) and *Sarcina* (Fig. 74, **16**).

The spherules known as micrococci exhibit no perceptible organization, but it is highly probable that they are differentiated into cell-membrane and cell-contents. They are found in liquids and in tissues, either isolated or arranged like strings of beads or "chaplets" (Fig. 74, **1***b*), or grouped in colonies (zooglœa, Fig. 74, **2**). On examination it is found that in these colonies or zooglœa the separate spherules are united by a gelatinous intercellular substance. Cohn affirms that this is nothing but

the swollen and thickened cell-membrane. Von Nencki affirms that it consists of mycoprotein.

With regard to their growth and increase, it is made out that the individual cells first elongate and then subdivide transversely. If the subdivided cells remain conjoined the result is a *diplococcus* (Billroth). If the process of subdivision goes on, the new cells remaining attached and in line, chains or chaplets are produced. If large numbers of spherules remain after subdivision within the swollen and continually enlarging membrane, the result is a mass of zooglœa.

The genus *Micrococcus* includes several species. These are distinguished partly by their morphological and partly by their physiological characters. In the first place the micrococci are of various sizes. When cultivated on a proper soil they form colonies of various types. Many of them as they multiply produce yellow, red, blue, green, or brown coloring matters. Lastly, the effects produced in the soil or liquid in which they grow are various ; nor do they all flourish on the same kind of nutriment. It is still doubtful whether the micrococci are motile. The oscillatory movements observed in them are probably to be regarded as Brownian or pedetic movements. Klebs believes that the zooglœa are contractile.

The genus *Sarcina* is very clearly marked. The globular cells divide crosswise, and the daughter-cells usually remain combined in tetrads (Fig. 74, **15**). Various species have been distinguished according to the size of the cells.

[Billroth and Klebs assert that micrococci may grow into rodlets or bacilli. It is not to be denied that some bacterial spherules become transformed into rods (Art. 185), but Cohn is probably right in maintaining that *Micrococcus* is a definite genus of constant form. Ziegler has cultivated *Micrococcus luteus*, a bacterium which develops on boiled eggs exposed to the air and forms yellow zooglœa ; and though the experiments were carefully made to that end, he could never obtain bacilli, but always micrococci. Experiments on parasitic micrococci seem equally to indicate that there is a genus of bacteria which forms globular cells only. It is not yet certain whether or not the micrococci produce spores. Koch thinks it unlikely. See also Ewart, "Proc. Roy. Soc.," xxvii.]

185. The **Microbacteria** are classed together as a single genus *Bacterium*. The principal species are *Bacterium termo* (Fig. 74, **3**) and *Bacterium lineola* (Fig 74, **5**). The first appears in the form of minute cylindrical rods, 0.5 to 1.5 micromm. in length, and appearing bright or dark according to the mode of illumination. Sometimes they remain at rest, sometimes move about more or less actively. From their manner of subdivision they are often found coupled in pairs ; they do not usually form chains or chaplets ; but are often grouped as zooglœa (Fig. 74, **4**), which are remarkable for the great abundance of the gelatinous intercellular substance. *B. termo* is very generally found in putrefying mat-

ters. *B. lineola* resembles *B. termo*, but it is larger in every way. It is found in water, in infusions, on potatoes, etc. The cells, which are from 3.8 to 5 micromm. in length, contain a clear bright substance interspersed with fine granules. In other respects the bacterium resembles *B. termo;* it swims about actively, moving forward and backward in curves, rotating or oscillating. At times it remains motionless. It forms continuous pellicles on the surface of liquids containing it.

When micrococci or microbacteria have exhausted the nutriment contained in the liquid in which they live, they fall to the bottom as a powdery precipitate.

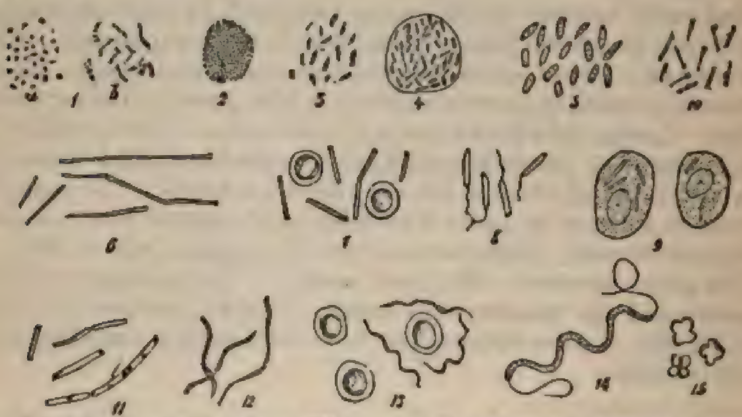

FIG. 74.—Various Forms of Bacteria. × 500 (in each case). 1, *Micrococcus septicus:* *a*, separate, *b*, in chaplets; 2, *Micrococcus diphtheriticus*, forming a zooglœa-mass; 3, *Bacterium termo;* 4, Zooglœa of *B. termo;* 5, *Bacterium lineola;* 6, *Bacillus subtilis;* 7, *Bacillus anthracis*, with red blood-cells; 8, Flagellate bacillus from the mouth; 9, *Bacillus lepræ* (Armauer Hansen); 10, Bacillus with terminal and medial spores, from a putrefying liquid; 11, *Bacillus malariæ* (Klebs), with spores; 12, *Vibrio serpens* (Cohn); 13, *Spirochæta Obermeyeri* ("spirillum" of relapsing fever); 14, *Spirillum volutans* (Cohn); 15, *Sarcina ventriculi.*

[As has been indicated in Art. 184, Billroth, Hallier, and Klebs maintain that the microbacteria represent merely a developmental stage in the life-history of the micrococci. Billroth ("Unters. über Coccobacteria septica," Berlin, 1874) believes that all bacteria belong to a single species of plants, the members of which are composed partly of round and partly of rod-like segments varying greatly in size. The round segments are the cocci, the rod-like segments bacteria. Each form may pass into the other on occasion; though they so far breed truly that for some generations cocci produce only cocci, and bacteria only bacteria. According to size we may distinguish them as micrococci, mesococci, and megacocci, and microbacteria, mesobacteria, and megabacteria. Megacocci may break up into micrococci. The plant which passes through all these stages Billroth calls *Coccobacterium septicum*. In the process of multiplication it develops a gelatinous envelope or gliacoccus. When this occurs at the surface of a liquid so that a pellicle is formed, he calls it petalococcus or petalobacterium. Masses of cocci enclosed in a cylindrical sheath of gliacoccus are called ascococci (Van Tieghem, "Bull. Soc. Botanique,"

1880). Coupled spherules are diplococci; chains or chaplets of spherules, streptococci; and, in like manner, he describes diplobacteria, and streptobacteria. Ray Lankester (*Quarterly Journal of Micros. Sci.*, 1873) also inferred from certain experiments of his that Cohn's forms are not really distinct. Haberkorn ("Bot. Centralb.," 10, 1882) maintains that Cohn's four divisions merely represent diverse species of a single genus. Billroth's view of the specific unity of all the bacterial forms has been discredited by later researches (*cf.* Tiegel, "Virch. Arch.," vol. lx.; Lister, "Trans. Roy. Soc. Edin.," 1875).

Klebs ("Arch. f. exp. Path.," iv.) divides the globular and rod-like bacteria into *Microsporina* and *Monadina*. He defines the *Microsporina* as small micrococci which in the resting state form well-defined and compacted balls; the several spherules being regularly deposited in layers and surrounded by only a small quantity of gelatinous matter. The peripheral spherules grow into minute motile bacteria, which tend to move away from the mass, and thus further the diffusion of the organisms through the nutrient liquid. The highest stage of their development is reached in the formation of a matted tuft of unbranched filaments. The monadina form loose balls, from which motile monads or vibrios break away. These grow into rodlets which are relatively short and broad; and these again subdivide; they probably increase also by conjugation. They then pass into a resting state, and lie quietly alongside each other. Lastly they break up into spherules; it is rare for them to form tufts or clusters. They require oxygen, and thrive better on albumen than on gelatine.

It is not yet certainly known whether *Bacterium termo* produces spores or not. It has been described as possessing *flagella* by Dallinger and Drysdale (*Month. Mic. Journ.*, xiv.), and by Koch ("Beiträge zur Biol.," 1877).]

186. The **Desmobacteria** (or Filobacteria) are cylindrical rodlets of varying length; some of them are thick, and some slender and delicate. Cohn describes a straight form which he calls *Bacillus*, and a wavy or curved form which he calls *Vibrio*. *Bacillus* increases by transverse subdivision, and frequently forms a long string (Fig. 74, 6), commonly referred to as a *leptothrix* (Hallier). It is not always easy to make out that the string is made up of distinct rodlets. In other cases bacilli form swarms. Many bacilli pass through both a resting state and a swarming state. Many are provided with a flagellum or cilium, which acts as an organ of locomotion (Fig. 74, 8). The best representatives of this genus at present known are *B. subtilis* (Fig. 74, 6), *B. anthracis* (Fig. 74, 7), *B. tuberculosis* (Fig. 80), and *B. lepræ* (Fig. 74, 9). The various specific forms are distinguished by their general size, and by the relation of their length to their breadth. Some of them are cut off square at the ends, others are rounded off or pointed. Even more marked differences than these become apparent when the various forms are cultivated in nutrient

liquids. "Cultures" of this kind have been made by Cohn, Koch, Klebs, Brefeld, Prazmowski, Lister, Naegeli, Buchner, Klein, and many others, and we have thus come to know something of the life-history of many of the varieties. Cohn bred the *B. subtilis* in hay infusions; Koch the *B. anthracis* found in the blood and tissues of animals suffering from splenic fever; and also the *B. tuberculosis* (Art. 206).

The life-histories of the different species differ in many details; but they usually agree in their main features. Features which thus constantly recur are—the longitudinal growth of the rodlets, their transverse subdivision and abstriction, and the formation of spores or gonidia. The life-history of *B. anthracis* is briefly as follows.

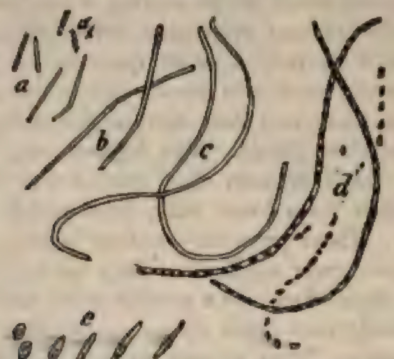

FIG. 75.—Development of *Bacillus Anthracis*. × 400. (From Koch.) *a*, bacilli from the blood; a_1, dead bacilli; *b*, bacilli cultivated for three hours; *c*, for ten hours; *d*, for twenty-four hours; spores are forming and the filaments are breaking up; *e*, germination of spores.

If the anthrax-bacillus be observed under proper conditions, it is found in a short time to grow lengthwise to a very considerable size (Fig. 75, *b*). Within twenty-four hours a string or filament is formed (Fig. 75, *c*), which may be ten or twenty times as long as the original rodlet. In ten or fifteen hours more the clear contents of the filament become granular. Then appear at regular distances small darker bodies, which grow in a few hours into larger highly refracting spores (Fig. 75, *d*). The filaments afterward break up, and the spores are set free. In favorable circumstances these spores may germinate and develop into bacilli exactly like those originally taken from the blood.

According to Koch, each spore consists of a bright body surrounded by an envelope of clear protoplasm. As the spore germinates the latter grows into a rodlet (Fig. 75, *e*). The researches of Klein, Brefeld, Prazmowski, Ewart, and others do not corroborate this account. They make out that the spore consists of protoplasm enclosed in a membrane. The rudimentary bacillus is developed not from the peripheral layer of the spore, but from its protoplasmic centre.

In addition to this mode of increase by spore-formation observed in cultivated bacilli, the rodlets multiply by transverse subdivision. This is especially the case in the blood of living animals.

As we have said, all bacilli have the power of forming spores. It is not, however, essential to the process that long filaments should be formed. Many bacilli produce spores without having undergone any marked increase in their length. The number of spores in each rodlet varies from one to three. They may occupy either a terminal or a medial position (Fig. 74, **10** and **11**).

Anthrax-bacilli cultivated on gelatine are never motile (Koch); they always form flakes or tufts made up of long, wavy, tress-like or twined filaments. The bacilli of hay-infusion grow out into long filaments in very young colonies only. When they become more mature and cause the gelatine to liquefy, they are seen in active movement at the centre of the colony, while round its periphery they stand in regular array all perpendicular to the surface and penetrating the firmer gelatine. The colony then looks as if it were surrounded by an aureole of rays. Other bacilli form colonies looking like tufted roots of trees; others again spread out in one plane and form mosaic designs.

[Cohn's and Koch's researches are published in the "Beiträge zur Biologie d. Pflanzen," vol. ii., and "Mittheil. a. d. kais. Gesundheitsamte," Berlin, 1881; Brefeld's are in the "Botan. Zeitung," 1878, and in "Botan. Unters. über Schimmelpilze," 1881; Klein's, Sanderson's, and Ewart's, in the *Quart. Journ. of Micros. Science*, 1878. Prazmowski asserts ("Unters. über d. Entwick. einiger Bacterien," Leipzig, 1880) that the germination of the spores of *B. subtilis* follows a different course to that of *B. anthracis*. The mature spore is oval, highly refracting, sharply defined, and surrounded by a transparent zone. On germination the spore becomes pale, and loses its lustre and its sharp contour. At each pole a kind of shading appears, the spore meanwhile beginning to move in a tremulous manner. After a time the contents escape laterally in the form of a minute cylindrical shoot, which grows into a rodlet; and this latter then proceeds to subdivide.

Prazmowski has also made out the life-history of the so-called *Clostridium butyricum* (Pasteur's *vibrion butyrique*, Van Tieghem's *Bacillus amylobacter*). It forms rodlets 9–10 micromm. long, which are seen alternately at rest and in moving swarms. Before fructification they increase in thickness and become more fusiform or pear-shaped. On germination the spore swells and begins to jerk about. The membrane at one end is absorbed, the germinal cylinder escapes, and as it grows proceeds to subdivide as before.

Kern describes a bacillus under the name of *Dispora Caucasica* ("Biolog. Centralb.," 5, vol. ii.), much resembling *B. anthracis*; it is, however, distinguished from the latter by its always exhibiting terminal spores at each end of the rodlets. When cultivated in milk this bacillus sets up a peculiar fermentation, which produces an agreeable drink much used in the Caucasus.

Brefeld distinguishes an external spore-membrane or exosporium

which is thrown off in germination, and an internal or endosporium which becomes the envelope of the germinal cylinder.

With regard to the term *leptothrix*, it is to be noted that all filaments or strings so named do not necessarily represent developmental stages of a bacillus. The filaments formed by algæ, for example, are also spoken of as *leptotriches*.]

187. The **Spirobacteria** are divided into two genera—*Spirochæta* (Fig. 74, **13**) with long, flexible, close-wound spirals; and *Spirillum* (Fig. 74, **14**) with short, stiff, open spirals. For the pathologist, *Spirochæta Obermeyeri* (**13**) and *Spirochæta denticola* are the most important species of the first genus. The former (often referred to simply as "spirillum") is constantly found in the blood of patients suffering from relapsing fever, during the paroxysms. The latter is found in the mouth and nose of persons who may be quite healthy or suffering from nasal catarrh. The length of the former is twice or thrice the diameter of a red blood-cell. It moves with extraordinary agility through the blood, and is therefore hard to see unless it be somehow fastened down or restrained. No structure has been made out in it.

No details are known of the life-history of *Spirochæta*. It plainly increases very rapidly within the body. It probably produces resting-spores.

The largest of all bacteria, *Spirillum volutans*, belongs to the *Spirilla* (Fig. 74, **14**). Apart from its size it is distinguished by its granular protoplasm and its pair of flagella. It sometimes moves about actively, sometimes lies quiescent. It is occasionally found in drinking-water. Two smaller forms, *Spirillum tenue* and *Spirillum undula*, also belong to this genus (Art. 207).

Biology of the Bacteria.

188. **Conditions of life.** All bacteria require to be supplied with certain definite nutritive substances if they are to develop normally. The requisite substances are partly inorganic, and partly organic (carbohydrates and albuminoids). The inorganic components are derived from salts containing sulphur, phosphorus, magnesium, and potassium. The requisite carbon and nitrogen are mainly derived from animal and vegetable matters. But bacteria have also the power of assimilating nitrogen from ammonia, urea, or even nitre, provided only the other mineral substances needed are also present, and in addition some appropriate organic carbon-compound, such as sugar.

These nutritive substances must be presented to the bacteria associated with a certain amount of water. None of the bacteria can develop without water, though many of them may be without it for a time and still continue to live. This is especially the case with bacterial spores. If the water contains no proper nutriment, or if the nutriment

is already used up, the bacteria cease to develop, and after a time die outright. But here, as when water is lacking altogether, it is possible for the bacteria to maintain life for a time. The spores are still more tenacious of life, and can hold out almost indefinitely. Free oxygen is absolutely necessary to the development of many of the bacteria ; others can do without it if they are otherwise favorably placed, and in circumstances where they can set up fermentation. The former kind, *e.g.*, *Bacillus anthracis* and *B. malariæ* (Klebs), have been called by Pasteur **aërobious** fungi. The latter, of which *Bacterium termo* and *Clostridium butyricum* are the best-known examples, are **anaërobious**. Pure oxygen is said to kill bacteria outright.

[Nägeli gives minuter details of the conditions of life of the various bacteria (" Die niederen Pilze," Munich, 1877, and " Untersuch. über die nied. Pilze," 1882). Pasteur, Joubert, and Chamberland have papers in the " Gaz. méd. de Paris," 1876, on the relations of bacteria to oxygen. Prazmowski asserts that, so far as concerns *Clostridium*, oxygen is not merely unnecessary but positively harmful. *B. anthracis*, on the other hand, dies if deprived of oxygen, breaking up into rounded fragments. Pasteur again affirms that the bacillus which gives rise to the " Pasteurian " septicæmia in rabbits, dies if exposed to the air. According to Koch (" Mittheil. a. d. k. Gesundheitsamte," Berlin, 1881), the anthrax-bacillus perishes if it is allowed to become dry ; while the spores may be preserved for years in the dry state. They may even be kept moist for a time without losing their power to germinate or to produce the specific infection.]

189. The **temperature** of the nutrient medium has great influence upon the development of bacteria. If the temperature be lowered, the effect is generally to slow and to weaken the vital processes, and ultimately to put an end to them altogether. As the temperature is raised, on the other hand, these processes become more and more active until a certain maximum is reached ; carried beyond this point they rapidly and suddenly cease, in most instances not to revive again. The maximum temperature which can be borne by fungi varies in the different species ; a few are capable of growth at 70° to 74° C. (Van Tieghem). The development of all kinds is stayed at a temperature of 5° C. They become stiff and immobile, but are not absolutely killed even by very extreme degrees of cold. The *rigor frigoris* sets in at different temperatures in different species ; in the case of *B. termo* at 5° C., of *B. anthracis* at 15° C. For *B. anthracis* the temperature most favorable to development is 30°–40° C.; at 42° C. development ceases. *B. termo* develops best between 30° C. and 35° C.

All bacteria and all bacterial germs are killed by boiling-hot water or steam, after exposure for a certain time. The spores are much more resistant than the bacteria. In dry air both may endure much higher temperatures. Spores, for instance, are not destroyed at a temperature

of 140° C. until after three hours' exposure. *B. termo* perishes at 65° C., if the temperature be kept up for a considerable time.

[Researches on the effect of temperature on the bacteria and their spores have been made chiefly by Eidam ("Cohn's Beiträge z. Biologie d. Pflanzen," vol. ii.), Koch, Wolffhügel, Gaffky, and Löffler ("Mitth. a. d. k. Gesundheitsamte," Berlin, 1881), Van Tieghem ("Bull. Soc. Bot.," 1881). The following are the chief results arrived at.

Bacterium termo passes into *rigor frigoris* at 5°, into *rigor caloris* at 40°. At 45° the ordinary putrid decomposition of albuminoids ceases to go on (Eidam).

Bacillus anthracis multiplies the more slowly as the temperature is lower, within certain limits. Between 30° and 40° growth and spore-formation are completed in twenty-four hours; at 25° this time is increased to thirty-five or forty hours. At 23° the spore-formation occupies forty-eight or fifty hours; at 20° seventy-two hours; at 18° it takes five days, at 16° seven days. Below 15° growth and spore-formation cease (Koch). Spores are still formed at a temperature of 42°. See also Sanderson and Ewart, *Quarterly Journal Mic. Sci.*, 1878.

Bacteria without spores, when exposed to hot air, cannot endure a temperature much over 100° for so long as an hour and a half. The spores of bacilli are only destroyed after three hours' exposure to a temperature of 140°. In the case of objects exposed to heat with a view to disinfection, it is noteworthy that the temperature penetrates very slowly. Objects of moderate size, such as bundles of clothing, pillows, etc., are not completely disinfected even when exposed for three or four hours to a temperature of 140° (Wolffhügel). Anthrax-bacilli perish when exposed to boiling water for two hours; when exposed to steam in a closed space ten minutes suffices. On the other hand, the peculiar bacillus found in garden-soil is not destroyed by this exposure. Superheated steam at 105° kills all bacterial germs. A jet of steam is more powerful than steam in a closed chamber. It will kill all kinds of germs in ten to fifteen minutes, and it readily penetrates the articles to be disinfected (Koch, Gaffky, Löffler). When using boiling water for disinfecting purposes, care must be taken that the heat is kept up long enough, *i.e.*, until all the parts are warmed up to 100°.

The effect of temperature in modifying the virulence of pathogenous bacteria will be referred to later on.]

190. Another factor of importance in regard to bacterial development is the **presence of foreign** or non-nutritive **substances** in the nutrient liquid. Many substances (like corrosive sublimate, bromine, iodine, and some acids) have a very powerful effect even in small quantity. They put an end to growth and fermentive action, or kill the organisms outright. Other substances have no injurious effect unless present in considerable quantity.

The fermentive action of the fungi leads to the formation in the nutrient liquid of substances which, when they reach a certain degree of concentration, may ultimately put a stop to the growth and multiplication of the fungi themselves. In alcoholic or lactic fermentation, for instance, the gradually accumulating alcohol or lactic acid ultimately brings the fermentive process to a standstill.

If nutritive matters be present in excess (or if, in other words, the supply of water be inadequate), the growth and multiplication of the fungi ceases in like manner. This is the reason why conserves of fruit made with sugar do not ferment, why condensed milk does not turn sour, and why dried or salted meat does not putrefy. By withdrawing water, or by adding substances which dissolve in the organic liquids, we are able to increase the proportion of solids to liquids in organic substances such as provisions, and so preserve them from decomposition by fungi. The quantity of water necessary for the development of fungi like bacteria and the yeast-plant is greater than in the case of the mould-fungi.

Horwath's and Reinke's researches ("Pflüger's Arch.," xvii., xxiii.) show that constant agitation of the liquid hinders the development of bacteria, and may even check their multiplication altogether.

A further factor of importance in bacterial development is the presence of lower orders of fungi in the nutrient liquid. As higher plants often encroach on and interfere with each other, so it is possible for bacteria, yeast-plants, and moulds to interfere and compete with each other for nutriment (Nägeli). A bacterium, which is thriving and multiplying in a given liquid, may be checked and ultimately killed merely by introducing another fungus which is still more at home in the liquid. Thus, if we introduce into a nutrient liquid containing sugar the germs of a number of fungi of different classes, the bacteria alone will multiply and set up lactic fermentation. If a half per cent. of tartaric acid be now added, the yeast-fungi alone will proceed to multiply, and alcoholic fermentation will begin. Add now from four to five per cent. of tartaric acid, and mouldy growths appear. The tartaric acid does not kill the other fungi ; it merely favors one more than the others. Thus it is that in grape-must it is only the yeast-fungi which flourish, though other germs are certainly present. Only when the sugar is all used up have the bacteria a chance to multiply, and then they set up acetous fermentation. Mould-fungi may then develop in the presence of the vinegar, and they consume the acetic acid. Lastly, when this is done, the bacteria reappear and set up putrefaction.

Even among the Bacteria themselves a like mutual interference and struggle for existence is observed. Micrococci may be thrust aside by microbacteria. Bacilli may be killed by *Bacterium termo*, when the supply of oxygen is insufficient for both.

It is also a point of importance, when there are various kinds of fungus-germs present, to know which kind is most abundant. If the

soil be equally well adapted for two or more forms, the form represented by the majority of germs will have the advantage.

[Koch and Wolffhügel have made very careful investigations into the action of various substances on the life and multiplication of bacteria. ("Mittheilungen, etc.," 1881). The subject has also been treated by Buchholtz ("Arch. f. exp. Path.," iv.), Schotte and Gärtner ("Deutsche Viertelj. f. öff. Gesund.," xii., 1880), Nägeli ("Die niederen Pilze," Munich, 1877 and 1882), Roberts ("Phil. Trans.," 1874), Hamlet (*Journ. Chem. Soc.*, 1881), and many others. The following results of investigation are worthy of note.

Corrosive sublimate has the most powerful effect on bacteria: an aqueous solution of 1:20,000 kills the spores of bacilli in ten minutes. A solution of 1:5,000 is thus a certain disinfectant, even when the time of exposure is very short. Mercuric sulphate is somewhat less active. Koch finds that an aqueous sublimate-solution of 1:300,000 puts a stop to the germination of bacterial spores.

Sulphurous acid does not take a high place as a disinfectant. Bacteria clinging to dry objects are killed by twenty to thirty minutes' exposure to an atmosphere containing 1 vol. per cent. of sulphurous acid. Spores of *B. subtilis* and *B. anthracis* are still capable of development after ninety-six hours' exposure to an atmosphere containing 5 to 6 vols. per cent. of sulphurous acid. Even when moist they are very hard to kill with it. It is thus an altogether untrustworthy disinfectant, and all the more because it has little power of penetrating compact masses or bundles (Wolffhügel, Buchholtz, Schotte and Gärtner, Koch, Buchner).

Carbolic acid in five per. cent. solution will kill the spores of the anthrax-bacillus in twenty-four hours. A three per cent. solution will not do so in the same time. The bacilli, however, are killed in a few minutes even by a one per cent. solution. A solution of 1:400 checks the development of bacterial spores. Vapor of carbolic acid at ordinary temperatures is without effect; at 55° C. it kills spores in two or three hours (Koch, *loc. cit.*; De la Croix, "Arch. f. exp. Path.," xiii.). Chloride of zinc in five per cent. solution has no effect on anthrax-spores—even when they have lain in it for a month (Koch).

Iodine, bromine, and chlorine are far more active than sulphurous acid. Bacilli cease to grow in presence of iodine in the proportion of 1:5,000, and of bromine of 1:1,500. Steam from bromine-water kills spores in twenty-four hours, from chlorine-water in two days. Iodine-water and chlorine-water kill spores in one day, a five per cent. solution of chloride of lime in ten days. Benzoic acid, sodium benzoate, potassium chlorate, and quinine have little effect on spores. The following substances, even in dilute solution, have a restraining influence on bacterial development: allylic alcohol; oils of mustard, peppermint, turpentine, and cloves; thymol; chromic, picric, hydrochloric, and salicylic acids; quinine. The effect is perceptible in solutions of 1:300,000 for

oil of peppermint, of 1:800 for quinine, of 1:75,000 for oil of turpentine.

All disinfecting agents should be used in aqueous solution. In alcohol or oil they are either inactive or enfeebled. Bacillus-spores still retain their power to germinate after lying for months in absolute alcohol. In water and in glycerine they may lie for weeks undestroyed.

Bacteria become less able to resist heat in presence of small quantities of acid. They are made more resistant by alkalies. For the effect of light on their development see Engelmann, "Rev. internat. Sci. biol.," 1882.]

191. **Influence on the nutrient liquid.** In the first place the bacteria, as they grow and multiply, withdraw from the nutrient liquid the elements they require for building up their cells. These elements are chiefly nitrogen, carbon, hydrogen, and oxygen, as also the mineral constituents mentioned in Art. 188. In the next place they set up marked chemical changes in the nutrient liquid. It is bacteria which superinduce putrid decomposition in albuminoid bodies; they transform sugar into lactic acid (as in soured milk); lactic acid into butyric acid (as when sourkrout ferments, or butter becomes rancid); sugar into a gum-like slime (as in "slimy" or "long" wine); and alcohol into acetic acid. Large quantities of material may in this way be very rapidly transformed.

When albuminoids undergo putrid decomposition, we have formed peptones and similar bodies; a certain putrid principle or poison (Panum), and bodies resembling ferments; sepsin (Bergmann and Schmiedeberg); nitrogenous bases, like leucin and tyrosin; amines like methylamine, ethylamine, propylamine; fatty acids, like formic acid, acetic acid, propionic acid, butyric acid, valerianic acid, palmitic and stearic acids, lactic acid succinic acid, etc.; aromatic matters, indol, phenol, cressol, pyrocatechin, hydroquinone, hydroparacuminic acid, and paroxyphenylacetic acid (von Nencki, Salkowski, Brieger); and lastly, sulphuretted hydrogen, ammonia, carbonic anhydride, and water. These products are the result partly of hydration, partly of reduction, and partly of oxidation.

The immediate cause of the process is unknown. Nägeli ("Die niederen Pilze," 1877), Pasteur, Lister, and others, regard the decomposition as the direct result of the vegetation of the bacteria. Decomposition and fungus are inseparable; the one ceases when the other is removed. Processes of this nature, set up by bacteria, are best distinguished as **fermentations.** Considered with respect to their property of setting up fermentation, bacteria are often described as "formed" or "organized" ferments. Bacteria have also the power of setting free certain substances which have a decomposing action like themselves, but are capable of separation from them, and are known as "unorganized" ferments. Such unorganized ferments can, for instance, change lactose into fermentable sugar, transform starch and cellulose into grape sugar, and render soluble coagulated albumen and other insoluble albuminoids. In consequence of such changes milk may undergo alcoholic fermenta-

tion, wood may become soft and rotten, damp bread turn sour, and insoluble albuminous matters be transformed into a putrid ammoniacal slime.

Under the influence of bacteria are also developed certain bitter, acrid, and nauseous products, of whose composition nothing is known (as when milk turns bitter). Now and again coloring matters are produced by them, red, yellow, green, blue, and violet. So bread may become covered with a blood-red film of *Micrococcus prodigiosus* ("bleeding" bread). Bandages and pus in wounds become blue from the presence of *Micrococcus cyaneus*. Boiled eggs exposed to moist air are often quickly covered over with a yellow film of *Micrococcus luteus*.

[The hypotheses proposed to explain fermentation, especially the alcoholic fermentation, have been very various. Some of them attempt to connect the process intimately with the vital activity of the cells which give rise to it; others seek to separate them. Liebig describes the process as a molecular motion transmitted by matter (the unformed ferment) already in a state of chemical motion (*i.e.*, in the act of decomposing) to other matters composed of elements in loose combination. Hoppe-Seyler and Traube ("Pflüger's Arch.," xii., 1875, and "Physiologische Chemie") imagine that the cells secrete certain unformed ferments, which produce decomposition by mere contact (or catalytically), without themselves taking part in the chemical changes they set up.

Pasteur ("Annal. de Chimie et de Phys.," 58, 64; "Comptes Rendus," 45, 46, 47, 56, 80; "Studies on Fermentation," London, 1879; Duclaux's "Ferments et Maladies," Paris, 1882) regards fermentation as immediately dependent on the activity of the living cells. Fermentation begins only when the supply of free oxygen to the cells is restricted. They then begin to abstract oxygen from the compounds contained in the nutrient liquid, and so disturb their molecular equilibrium.

Nägeli's physical (or molecular) theory ("Abhand. d. bayr. Akad. math. physic. Cl.," xiii., p. 76, 1879) supposes that the natural motions of the molecules and atoms of the various constituents of the living cell-protoplasm are transmitted mechanically to the fermenting matter. The protoplasmic constituents remain chemically unchanged, but the molecular equilibrium of the fermenting matter is disturbed, and disintegration results. Nägeli's theory emphasizes strongly the dependence of the fermentive process on the life of the cells, and is thus in harmony with our general view that all vital processes are ultimately cellular.

The power of exciting fermentive decomposition in nutrient liquids is very probably possessed not merely by bacteria and yeast-cells, but also by the cells of higher organisms, as of man. Voit ("Physiologie des Stoffwechsels," Leipzig, 1881) refers the disintegration of the soluble albumen circulating through the system to fermentive action of the tissue-cells. Pasteur has shown that in proper conditions fruits and leaves may exhibit fermentive properties.

The chemical changes occurring in the putrid decomposition of the albuminoids have been studied by Nencki, Salkowski, Brieger, and Hiller. See Hiller, "Die Lehre von der Fäulniss," Berlin, 1879 ; Nencki, "Zersetzung der Gelatine und des Eiweisses bei der Fäulniss mit Pancreas," Berne, 1874, and articles in the "Journ. für prakt. Chemie," "Journ. für physiol. Chemie," and "Bericht. d. deutsch. chemisch. Gesell.," 1876–82 ; Salkowski, articles in the "Bericht. d. d. chem. Ges.," and "Zeitsch. f. physiol. Chem.," of the last year or two ; Brieger, "Zeitsch. f. physiol. Chem.," ii., iii., iv., and "Zeitsch. f. klin. Med.," iii.; Gautier and Étard, "Comptes Rendus," 1882.

The quantity of oxygen present has an important influence on the products formed in bacterial decomposition. Pasteur asserts that fungi which grow in presence of oxygen set up chiefly oxidative changes. Those which can multiply in the absence of oxygen give rise to non-oxidative decompositions. Hoppe-Seyler ("Ueb. d. Einfluss des Sauerstoffes auf Gährungen," Strasburg, 1881) supports this view by his observation that when oxygen is abundantly supplied to the yeast-plant the disintegration of sugar into alcohol and carbonic anhydride is retarded, and volatile acid bodies are produced in abundance. If bacteria in an albuminous liquid be well supplied with oxygen, products like indol, hydroparacuminic acid, and sulphuretted hydrogen (which are largely formed when oxygen is wanting), entirely disappear. The oxygen oxidizes them as they are produced ; the primary products of the fermentation at once undergo further change.

On pigment-producing bacteria see Cohn and Schroeter, "Beiträge z. Biol. d. Pflanzen," vol. i.]

192. Fermentation and putrefaction can only take place in the presence of the corresponding fungi, and the amount of decomposition produced depends on the quantity of fungi present. It does not, however, follow that each kind of decomposition is due to a single specific fungus, nor that one fungus may not give rise to more than one kind of decomposition. We cannot as yet define with certainty the kinds of decomposition which correspond to each species of fungus. We know, however, that ordinary putrid decomposition occurs under the action of *Bacterium termo ;* while Cohn asserts that micrococci do not give rise to putrid change, but to changes of another kind. The butyric fermentation is said to be chiefly due to the presence of *Clostridium butyricum.* Anthrax-bacilli generate ammonia in the nutrient liquid. In most putrefying substances we find bacteria of several species.

Nägeli affirms that it is possible by cultivation so to alter the properties of a bacterium that it no longer has the power to produce the changes originally associated with it ; while it assumes the power of calling forth fermentations of a different kind. Thus the bacterium which produces the lactic acid fermentation may, he says, be cultivated in saccharated extract of meat in such a way that at first it produces in

milk an ammoniacal decomposition only; and it does not resume its power of generating lactic acid until after several generations. If this be so we may perhaps infer that within certain limits the physiological properties of a bacterium may be transmuted; or at least that, by change of condition, one or other of several potential functions may be called into activity. The facts have not, however, been sufficiently confirmed.

[We have said that fermentation and putrefaction are always due to fungi; but we do not thereby deny that other kinds of decomposition may affect organic substances in which fungi play no part. Such changes do in fact occur. They usually take the form of slow oxidation or combustion, in which carbonic anhydride, water, and (in nitrogenous substances) ammonia, are formed. Such slow changes are set up when organic matters are in contact with water and atmospheric air. They also, of course, occur in the living organism. In dead organic matters the process corresponds in part to what is called "dry rotting" or "mouldering."

Brieger ("Zeitsch. f. klin. Med.," iii.) thinks that the various aromatic products of the putrefaction of albumen are equally well obtained whether it is set up by the addition of sewer-mud or of pancreas. The essential factors are the duration of the putrefactive process, the temperature, and the amount of oxygen present. The albuminoids undergo the same changes in the intestine as they do in artificial putrefaction brought about outside the body. The same series of changes are also set up in putrid pleurisy and bronchitis, and in pulmonary gangrene.]

193. **Bacteria without and within the body.** If the facts already cited be duly considered, it will appear very probable *à priori* that the diffusion of the bacteria is enormously wide. Matters on which they can grow and thrive are found almost everywhere. We might especially expect to find them wherever dead organic substances occur, either in solution or at least associated with a certain amount of water. This expectation is fully confirmed by experience. Bacteria are found in all waters, whether flowing or stagnant, in all liquids that can ferment or putrefy, and in all vegetable and animal tissues that are sufficiently moist.

Koch's researches have shown that the surface soil or mould is extraordinarily rich in bacterial germs. It is surprising to learn that these are chiefly the germs of bacilli; but micrococci are also found. In soils soaked with midden-runnings the micrococci are more numerous than the bacilli. If the soil become very dry, the micrococci disappear while the bacilli persist. This is due to the fact that the resting-spores of bacilli are very tenacious of life. The micro-organisms present diminish rapidly as we go deeper. At the depth of a metre they seem entirely absent. Spring-water coming from a depth contains hardly any.

But we have by no means exhausted the field of their distribution. When liquids containing fungi are violently shaken or broken into spray,

the fungi pass into the air. This happens also when such a liquid dries up, or when a solid nutritive substance is broken up or disintegrates. If in the latter cases no substances are present which agglutinate the bacteria into a compact mass, they may pass into the air in immense numbers. Owing to their extreme smallness and lightness (Nägeli estimates the weight of small moist bacteria at one ten-thousand-millionth (10^{-10}) of a milligramme) they are carried about by the faintest breath of air. In this way they must of course very often reach and rest on bodies which can offer them no nutriment. But they must also often fall on a fit soil, and then proceed to grow and multiply afresh. Circumstances in general are in fact so favorable to the bacteria, that we find them or their germs almost everywhere; but chiefly where the presence of organic matters, moisture, and warmth go to favor their multiplication.

[Nägeli ("Die niederen Pilze," Munich, 1877) asserts that fungi can only pass into the air when their nutrient liquids dry up. Soyka ("Münch. acad. Sitzungsber., math.-phys. Cl.," 1871) has shown that bacteria may be swept out of liquids that contain them by gentle air-currents. Buchner ("Ueb. d. Beding. d. Ueberganges von Pilzen in d. Luft u. üb. d. Einathmung derselben, Zur Aetiol. d. Infectionskrankh.," Munich, 1881) disputes Soyka's conclusions. He maintains that even strong currents of air are insufficient to sweep bacteria from a liquid; and that even in the case of dried-up masses containing fungi, the fungi are not set free unless the surface is actually broken. Ziegler agrees rather with Buchner's view.

Nägeli further thinks that very slight upward air-currents are enough to prevent floating bacteria from settling down. The condensed watery vapor that surrounds them tends to maintain their buoyancy. Friction also retards their fall. See Soyka, "Ueb. Canalgase als Verbreiter epidem. Krankh.," and "Ueb. Richtung und Stärke d. Luftzuges in Sielen, Deutsche Viertelj. f. öffent. Gesundh.," xiv., 1882; and "Ueb. d. Natur und d. Verbreitung d. Infectionserreger, Zur Aetiol. d. Infectionskrankh.," Munich, 1881; Nägeli, "Untersuch. üb. nied. Pilze.," Munich, 1882.

Wernich ("Cohn's Beit. z. Biol. d. Pflanzen," iii.) has shown that air-currents may sweep off bacteria from moist fungus-masses adhering to the surface of solid bodies. Researches on the bacteria and bacterial germs found in the air have been published by Cohn (*loc. cit.*), Miquel ("Des bactéries atmosphériques," "Gaz. méd. de Paris," 30, 1880), Wernich ("Virch. Arch.," vol. lxxix.), Tyndall ("Floating-matter of the Air," London, 1881); Cunningham ("Microscopic Exam. of Air," Calcutta, 1874) gives an excellent summary of previous observations. On bacteria and their germs in the soil, see Koch (*loc. cit.*), and Ceci ("Arch. f. exp. Path.," xv.).]

194. Consideration of the wide-spread occurrence of the bacteria and their peculiar vital properties will already have raised the question

whether these micro-organisms may not have the power of exciting more or less grave disturbances in the human system, provided they obtain an entrance into it. We have seen that almost all fluids contain bacteria or their germs, unless they are actually poisonous or are "sterilized" by appropriate means, such as by boiling. Micro-organisms are also frequently found in solid organic matters. In view of this it would seem that we cannot avoid swallowing numbers of bacteria with our food. Moreover, we frequently eat articles which are in a state of partial putridity or fermentation (such as cheese and milk); in this state they of course contain numerous bacteria. The alimentary tract must thus be reached by enormous multitudes of bacteria, together with the products of decomposition which they set up.

This is, however, by no means the only way in which we come into intimate relation with these organisms. The air always contains a greater or lesser number of them. In breathing we draw them into the lungs, and they settle in the bronchi or alveoli.

Lastly, all parts exposed to the air come into contact with bacteria, the unwounded skin as well as the wounded or abraded skin.

What becomes of all these organisms? The greater number undoubtedly pass out of the body again. It is hardly possible that any can penetrate into the deeper tissues through the uninjured skin. Those which settle on the mucous membranes are certainly for the most part not absorbed, but are thrown off after a longer or shorter time. This is, however, not always the case. Experience shows that, in special circumstances, bacterial invasion of the system may actually start from the mucous membrane.

What is the exception in the case of mucous membranes is the rule in the case of matters inhaled into the lungs. Experiment shows that fine corpuscular or particulate matters are very quickly taken up by the lymphatic capillaries of the lungs, and are so carried into the lymphatic glands, or it may be into the blood. Wounded surfaces are in like manner quick to absorb such corpuscular bodies.

Resuming what we have said, we may put it generally that bacteria of various forms may reach, not only the surfaces of the body which are directly accessible from without, but also at times the deeper structures, if circumstances favor their penetration.

[The question whether bacteria occur in the healthy body seems easily answered from such general considerations, though it is one which has been much disputed. Bacteria are perpetually entering the body with the food we eat and the air we breathe. They must, therefore, be at times found in the tissues, especially in places where access is direct. The fact that they are not easy to demonstrate is readily explained. It must be only a small number that can multiply in the tissues they have penetrated; the majority must quickly perish. See Nencki, "Journ. f. prakt. Chemie," 1879; Weissgerber and Perls, "Arch. f. exp. Path.," vi.;

Rosenbach, "Deutsche Zeitsch. f. Chir.," xiii.; Leube, "Zeitsch. f. klin. Med.," iii.; Sternberg, "Stud. Biol. Lab.," Baltimore, 1881; Lister, "Trans. Roy. Soc. Edin.," 1875. Leube, Lister, Roberts, and others have been unable to find living bacteria in healthy urine. This would indicate that the greater part of the bacteria which penetrate into the body are destroyed.]

195. If the bacteria were inert corpuscular elements, incapable of multiplication, we should have little more to say concerning their significance to the human organism. We should merely have to point out that they are in part taken into the body at certain points, are carried about hither or thither within it, are deposited here or there as innocuous substances, and sooner or later are destroyed or cast out again through the liver, kidney, or other secreting organ. As a fact this is what really happens with regard to some of the bacteria. Even when they pass through the bronchial glands from the lungs into the blood, they have no more significance than any other like minute foreign matters, such as occasionally circulate in the blood without causing disturbance. These are simply deposited and destroyed, or excreted. Thus the *Micrococcus luteus* may be introduced in considerable quantity beneath the skin of a rabbit, without inducing any serious affection either of the tissue or of the system generally. The bacteria which are thus innocuous may easily be indicated from previous considerations. They are such as cannot find within the human body the conditions favorable to their development.

This is unfortunately not the case with all bacteria. There are some which find their appropriate soil in the perfectly healthy organism, and in it they grow and multiply. Others are unable to settle in a perfectly healthy body; they can only develop when the physico-chemical constitution of the tissues is morbidly altered so as to correspond with their requirements.

The forms of bacteria that have the power of gravely affecting the system, whether it be healthy or diseased, are described as **pathogenous bacteria**.

[It is manifest from the above that the determination of the vital properties and conditions of the different bacteria is a matter of the greatest importance. This knowledge would enable us to combat earlier the development of bacterial disease, and the injury it produces. It would further give us the necessary hints for preventing its invasion; for we should know where to seek the bacteria and how to destroy them or render them harmless. Our knowledge in this respect is unfortunately still defective. There are but few species of bacteria whose life-history we know with any exactness of detail.]

196. The factors which determine the invasion and the course of development of bacteria within the human body are two. On the one

hand, the bacteria must be endowed with certain vital properties of a special kind ; on the other hand, there must be a predisposition on the part of the system.

Our present knowledge does not yet allow us to specify accurately the properties which an infective bacterium must possess. We can only say in general—that it must find within the body and in proper combination all the conditions necessary for its growth and multiplication. Thus the temperature of the body must be such as favors its development ; it must be able to abstract fit nutriment from the tissues in which it settles ; it must nowhere encounter substances which check or injure it.

Investigations into the bacterial affections have shown that very slight chemical changes in the constitution of a tissue are often enough to determine whether a given bacterium can develop in the tissue or not. In other words, the significance of this factor of predisposition is greater than it may have appeared at first sight. Now and then, of course, the predisposition is due to very obvious alterations in the tissues. For instance, we find that many cases of bacterial invasion depend on the formation of a local necrosis or wound, in which the fungus can settle and develop. In other cases some grave disturbance of the circulation may lead to a failure of resistance on the part of the tissue. These instances are, however, matched by others in which the anatomical basis of the predisposition is beyond our power to discover. We know, for example, absolutely no reason why—of two individuals exposed to the infection of measles, scarlatina, small-pox, typhus, or tuberculosis—the one should be taken with the disease and the other left. The factors which decide the matter in such cases are plainly such as at present escape our notice, either from their apparent slightness, or because they are not such as our tests can discover. Yet they doubtless consist in very real and very special differences in the condition of the tissues. Many of the bacteria can only come to development within the human body on rare occasions, as their usual habitat is without it. Others only meet with fit conditions for their existence and growth within the body, and do not multiply at all without it.

[The respective parts played by the inherent properties of the bacterium and the predisposition of the tissues to invasion have been illustrated by many observations both clinical and experimental. If a mass of bacteria of different forms be introduced into an animal's body, some of the forms develop and lead to certain tissue-changes, others perish inert. If a similar mass be injected into an animal of a different kind, the bacteria which develop are not the same as in the first instance. Koch ("Aetiologie der Wundinfectionskrankheiten," Leipzig, 1878, "Traumatic Infective Diseases," London, 1880) has shown that there is a fungus which brings certain death to one species of mouse, while it is entirely inactive when introduced into another species of mouse. Mice are highly susceptible to the infection of anthrax ; rats enjoy an almost per-

fect immunity. The poison of "rabbit-septicæmia" kills rabbits and mice with unfailing certainty; guinea-pigs and rats are unaffected by it; sparrows and pigeons again are highly susceptible. The *spirillum* of human relapsing fever will develop only in monkeys among the lower animals. Animals of the same species, but differing in age, have different degrees of susceptibility. Young dogs are easily infected with anthrax, old ones are not (Koch). We cannot at all tell on what circumstances immunity of this kind can possibly rest. Similar examples are easily obtained (Arts. 204, 206). The majority of the infective disorders are in fact limited each to a few species of animals or to a single one.

Differences also exist in respect of the diffusion of the bacteria through the body. The fungus, which in one kind of animal brings about a fatal general disease, may in others produce a merely local and non-fatal disturbance. Even the point of entrance of the bacteria into the body has its importance. A rabbit inoculated with bacteria in the back of the neck may die, while inoculation of the ear is followed by a simple local affection.

Rossbach has quite recently announced ("Centralb. f. med. Wiss.," 5, 1882) that injection of papayotin into the vessels is followed by a rapid development of micrococci in the blood, so that in two hours the blood in the heart is found to be swarming with them. If this observation be confirmed, it would seem to show that the composition of the blood is so altered by the unorganized vegetable ferment that germs can proceed to develop in it which before were unable to do so. In other words, that the action of a chemical substance has called forth a special predisposition.

Rosenberger ("Centralb. f. med. Wiss.," 4 and 41, 1882) observed a like result after the injection of sterilized septic blood. The animals died of septicæmia, bacteria being developed. If the injected liquid were really sterilized, we can only interpret the observation as showing that the septic matter so altered the blood and liquids of the animals as to make them predisposed for the development of micro-organisms. The experiments do not, however, seem quite free from objection. In 1869 Semner communicated similar results, which he obtained with the use of sepsin prepared from yeast ("Viertelj. f. wiss. Veterin.," xxxii.).

Boser maintains that the most essential condition for the settlement of bacteria in the body is their adaptation to the quantum of mineral salts present in the blood and tissues. This can hardly be a sufficient condition.]

197. The healthy organism is always beset with a multitude of **non-pathogenous bacteria.** They occupy the natural cavities accessible from without, and especially the alimentary canal. They feed on the substances lying in their neighborhood, whether brought into the body or secreted by the tissues. In so doing they set up chemical changes in these substances.

While the organs are acting normally, these fungi work no mischief to the tissues in which they lie, or to the system generally. The products of decomposition set up by such non-specific micro-organisms are either harmless, or are conveyed out of the body before they begin to be active.

Settlements of this kind may, however, become of importance if the bacteria proceed to develop to any unusual extent. This happens when the contents of the natural cavities in question remain unchanged for any great length of time, or when (as in catarrh) the normal secretion undergoes some alteration. The products of bacterial fermentation may then accumulate to an excessive amount, and products may also be formed which do not normally occur. Thus, when the contents of the stomach are not passed on, and become as it were stagnant, an abnormally acid fermentation may be set up. If the chyme is retained over-long in the small intestine, the aromatic products of albuminoid putrefaction will gather in excessive quantity. So, too, we may have decomposition in the stagnating secretions of the bronchi, prepuce, etc. All these changes react harmfully on the tissues and may set up inflammation, not unfrequently ending in suppuration and necrosis. Moreover, the system in general may suffer by absorption into the blood of the soluble products of decomposition.

The latter contingency is not to be lightly regarded. Though we may partake with impunity of many fermenting or decaying substances as food, we must not think that all the products generated by the non-pathogenous fungi are equally harmless. Highly poisonous substances are formed in many of the bacterial decompositions. One of the most speedily fatal of diseases, septicæmia, is due to poisoning of the system with the products of bacterial putrefaction, or sepsis. Cadaveric poison, the poison of decaying fish, sausage, cheese, mussels, etc., are very probably the chemical products of special forms of putrefaction. We unfortunately know but little, in some cases we know nothing, of the substances which have this poisonous character. Bergmann and Schmiedeberg have, it is true, prepared their so-called "sepsin," and Panum his "putrid poison," from decaying substances; but we do not know the composition of these bodies, and they are certainly not the only poisons of the kind.

Putrid or septic poison may be absorbed by wounds as well as by mucous surfaces. Septicæmia, which has just been cited as an instance of septic poisoning, is generally due to wound-infection. It is due to the absorption of products of bacterial decomposition formed in a wound contaminated by bacteria (Art. 204). This is especially apt to happen when necrosed tissue exists in the wound, for this affords the bacteria a suitable soil for their development.

[The poisonous action of putrid matters is fully discussed by Hiller in "Die Lehre von der Fäulniss," Berlin, 1879. He gives full references to the literature of the subject. Hiller lays special stress on the fact that

in the septic process it is not simply the bacteria themselves that do mischief, it is the products of their action which act so as profoundly to alter or even to destroy outright the tissues exposed to them. If the infection become generalized, it is almost always due to intoxication of the system with unorganized chemical substances.

Panum's paper just alluded to is in "Virch. Arch.," vol. lx.; Bergmann's is a work called "Das putride Gift und die putride Intoxication," Dorpat, 1866. Wolff ("Virch. Arch.," vol. lxxxi.) has lately taken up the question. On the absorption of putrid matters by the alimentary canal, see Salkowski, "Centralb. f. med. Wiss.," 46, 1876, and "Berichte d. chem. Gesells.," x., 1877; Nencki and Brieger, *ibid.;* Brieger, "Zeitsch. f. phys. Chem.," ii., "Zeitsch. f. klin. Med.," iii.; Bollinger, "Ueber Fleischvergiftung, intestinale Sepsis, und Abdominal-typhus, Zur. Aetiol. d. Infection," Munich, 1881.

It is possible that harmless colonies of bacteria may become dangerous if they are removed from their normal seat to other regions. Thus the saliva, when it contains bacteria, may excite violent inflammation if it reaches the bronchi or alveoli of the lungs.]

198. **Pathogenous bacteria** have the power of settling, not merely in the ingesta and secretions or in dead tissue, but also in living tissue. This happens chiefly in the mucous membranes and in the lungs. The uninjured skin is protected against invasion by the horny epidermis.

Many of the bacteria can settle in perfectly healthy mucous membranes. In the case of others we must imagine that they do not find a proper soil for their development, unless the mucous membrane is injured or altered. Of course, injury or alteration of this kind may serve to make the outer skin, or any other accessible tissue, the starting-point of a bacterial invasion (wound-infection). All that is necessary is that a bacterium should reach a spot that affords the conditions for its development. If this occur, it multiplies and forms colonies or swarms. These may, according to the species of the fungus and the nature of its soil, remain in aggregation forming heaps or masses, or may spread through the tissues. Such a settlement is never without effect on the affected tissues. The bacteria may force their way into the substance of the constituent elements, and especially into the tissue-cells, which are sometimes found to be crammed with bacteria.

The effect of the invasion is not always at once apparent, even under the microscope. The cells attacked by the fungi often appear quite uninjured; in other instances they are seen to be altered. The epithelial cells swell up (Fig. 76, *c*) and liquefy, or degenerate into flaky homogeneous lumps, or turbid denucleated masses. Often they break down into granular detritus. The nucleus is broken up, or swells and disappears (Fig. 76, *c*). The fibrous elements of the connective tissue degenerate like the epithelial cells. The ground-substance alters at the same time. It becomes turbid, loses its structure, and ultimately dissolves.

In general terms we may say—that local settlements of bacteria will sooner or later bring about degeneration and necrosis of the affected tissue. When this may occur, and how widely it may spread, are circumstances depending on the nature of the bacteria and of the tissue.

The processes we have considered are not without their influence on the circulation. The direct action of the bacteria, and the influence of the chemical changes they set up, tell at length on the vessel-walls within the affected region. The result is to disturb the circulation in various ways, chiefly in the way of inflammatory exudation and hemorrhage. In some instances the circulation is stopped altogether, and the preservation of the affected tissue is then impossible.

FIG. 76.—Section containing Colonies of Micrococci from the Vocal Cord of a Child. × 200. *a*, epithelium; *b*, connective tissue of the mucous membrane; *c*, swollen degenerated and denucleated epithelial cells; *d*, layer of micrococci; *e*, inflammatory small-celled infiltration of the degenerated epithelium and of the fibrous structures.

The inflammatory process set up by bacterial action (Fig. 76, *e*) may be of very different intensity and extent in different cases. It may be slight and transient, or it may be severe and issue in suppuration and necrosis. Not unfrequently a more or less perfect granulation-tissue is formed as a result of the inflammation, as in tuberculosis. The extravasated cells often take up the bacteria into their substance.

199. The inflammation excited by the presence of bacteria often results in a great aggregation of living cells in the tissue affected. These may so act as to repel the continued advance of the fungi, which straightway perish, and the affection issues in healing and cicatrization. The fixed tissue-cells of the region may likewise act so as to check the development of the bacteria, and may further suffice to make up any loss of tissue by their regenerative activity. If this does not happen the bacterial invasion continues to advance.

The bacteria spread first into the surrounding tissues, passing along the natural lines of division. Then they break into the lymphatics, and

often into the blood-vessels also. If they can live in lymph or blood they go on multiplying; if not they perish. Many bacteria, like the micrococcus of erysipelas, flourish best in the lymphatics. Others, like the anthrax-bacillus, are more at home in the blood.

The extent to which the bacteria can spread within the lymphatic system is subject to no general rule. Many of them make a halt at the first gland they come to. Others pass beyond, and finally reach the blood-vessels by way of the thoracic duct. Their path is generally marked by degenerative and necrotic changes, and by the inflammatory reaction they excite. The degree and amount of these changes are determined partly by the nature of the bacteria, partly by their number.

They reach the blood either through the lymphatics or directly. In the latter case the walls of the veins in the invaded region are penetrated by the fungi, or they pass into the veins from the capillaries. Once in the current they are carried on by it to remote parts. Many of them

FIG. 77.

FIG. 78.

FIG. 77.—Micrococcus Septicus in Hepatic Capillaries; Necrosis of the Liver-cells. × 350.
FIG. 78.—Bacillus Anthracis; Liver-cells unaffected. × 350.

perish in the blood, others again increase and multiply. Of the latter some (anthrax-bacillus) thrive best in blood that is flowing; others (tubercle-bacillus, pyæmic micrococcus) prefer blood that is at rest, that is to say, they only grow when they have come to a standstill in some venule or capillary. It depends on the properties of the fungus, which of these events takes place; just as do the changes it calls forth in the course of its multiplication.

The tissue-changes are the slightest in the case of bacteria which circulate and multiply in the blood (Fig. 78). Bacteria which settle in the smaller vessels give rise, on the other hand, to degenerations, necroses (Fig. 77 and Fig. 79, *c*), inflammations (Fig. 79, *d*, *e*), and hemorrhages.

The spot where a lodgement takes place is mostly matter of chance; but it is to be noted that a bacterium may not be able to settle in every spot indifferently. One part of the vascular system may be more favorable to it than another. Many bacteria remain and multiply within the vessels. Others escape from them, and when the surrounding tissue is suitable they may multiply in it, and set up changes resembling those produced at the point of first invasion (as in tuberculosis).

[References: Frisch, "Exp. Studien über d. Verbreitung der Fäulniss-organismen in d. Geweben," Erlangen, 1874; Koch, "Traumatic Infective Diseases" (Syd. Soc.), London, 1880; Perls, "Lehrb. d. allg. Path.," ii.

We should mention, with regard to the spread of bacterial infection within the system that the mode of invasion and the number of the fungi present are points of importance. If mice or guinea-pigs be inoculated

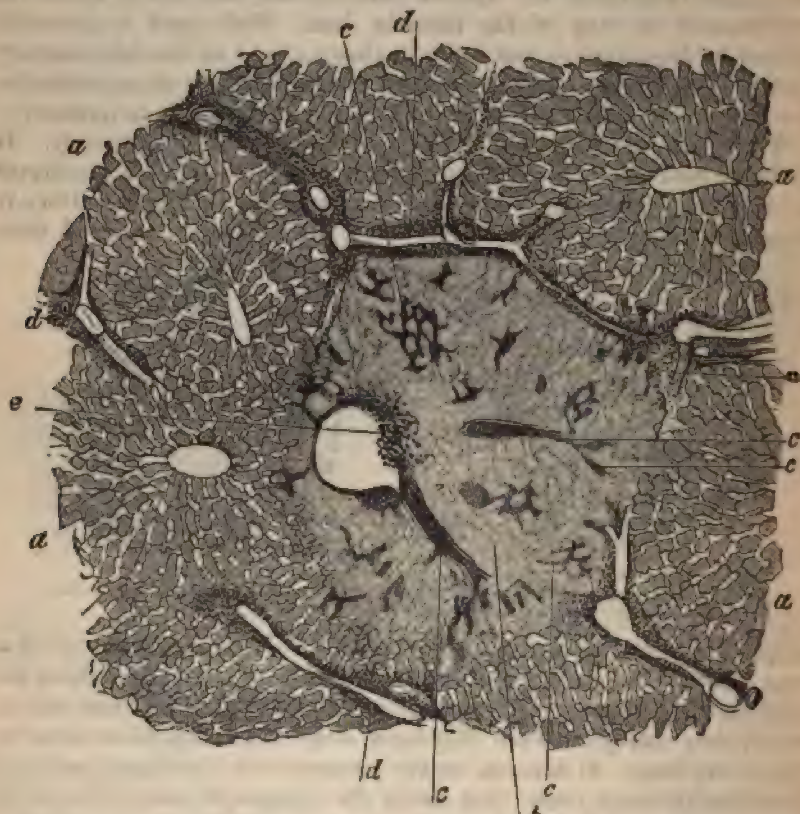

FIG. 79.—Hepatic Abscess: first stage. × 40. (Bismarck-brown staining.) *a*, normal lobules; *b*, necrosed lobules; *c*, capillaries filled with micrococci; *d*, small-celled infiltration of the periportal tissue; *e*, aggregation of small round-cells in a vein, into which opens an intra-lobular venule crammed with micrococci.

beneath the skin with a few œdema-bacilli, the resulting affection is merely local. If the bacilli be numerous the animals die of a general disorder. The bacilli of anthrax and those of "rabbit-septicæmia" may be injected in small quantity into the ear of a rabbit without causing its death. In the quantity ordinarily used in inoculative experiments they are always fatal.]

200. The facts just given (Arts. 198, 199) regarding the spread of bacterial infection within the system are derived from observations on

pyæmia, erysipelas, anthrax, and tuberculosis. The greater number of the diseases now referred by many to the action of bacteria (such as typhoid, relapsing fever, diphtheria, the exanthemata, croupous pneumonia, acute atrophy of the liver, cholera, etc.) are as yet too little known to enable us to give the corresponding details for them. We do not exactly know how the poison finds entrance, where it is multiplied, and in what manner it spreads. We only know that in these affections we find at certain times in the blood or tissues definite bacterial forms; and we believe that they are the exciting cause of the disease. If this belief be correct, we must admit that many kinds of bacteria have the power to penetrate into the blood and other juices without leaving any traces at the point of entrance. This supposition is confirmed by the fact that in anthrax we are often unable to detect the point of entrance of the bacilli. In the case of these diseases we must likewise assume, as in the case of the others, that the bacteria find access through the mucous membranes or lungs, or through open wounds if any exist. Once the bacteria have entered the body they multiply in the blood or in some tissue, spread through the system, and call forth the special changes characterizing the several diseases. It is worthy of remark that each poison has a corresponding special group of tissues, in which its mischievous effects are invariably and especially apparent. The anatomical changes produced in these diseases, as in the others, are of the nature partly of degeneration and necrosis, partly of inflammation or hemorrhage. Proliferous changes in the tissues may also ensue as secondary to the former.

201. We are not yet in a position to formulate a **theory of bacterial action** that will apply to all cases. The researches of the last year or two have, however, enabled us to form some picture at least of the way in which bacteria affect the several tissues and the system in general.

The pathogenous bacteria are parasites which draw their nourishment from man's body. They withdraw this nourishment only from the tissues among which they are growing and multiplying. The effect of this withdrawal is in general not very grave. It can only become dangerous to life when the bacteria multiply within the circulating blood and withdraw from it the indispensable oxygen it contains. The withdrawal of nutriment is not, however, the only result; it is seldom even the most important. Investigations show that the vital activity of the bacteria of necessity sets up extensive chemical change in their own nutrient materials. These changes are partly due to their direct action (Art. 191), partly to the action of the unorganized ferments which they form. Lastly, in the course of these changes, matters are produced which act as poisons upon the system. This effect of the bacteria on their nutrient fluids, and the production of poisonous matters, have much more to do with the genesis of the symptoms in most of the microparasitic affections than has the mere withdrawal of nutriment.

The influence of such factors is manifested in disturbances of the functional, formative, and nutritive activities of the organism. These

activities are the expression of the cell-life of the tissues; hence the statement that bacteria disturb the vital actions of the tissue-cells. In Art. 81 we compared the life-history of the tissue-cells with that of the bacteria. We may not inopportunely refer to the comparison once more in this place. The nutritive activity of the tissue-cells is not confined to the replacement of used material by the absorption and assimilation of new material. Like the bacteria, the tissue-cells act catalytically on their surroundings, partly by fermentive action (Art. 191), partly by the formation of unorganized ferments. Many cells have in addition the power of setting up synthetic processes.

When bacteria proceed to multiply within a tissue, a double influence is brought to bear on the common nutrient medium; the bacteria enter into conflict with the tissue-cells. We do not, of course, know in what exact way this conflict is carried on. But we may believe that the bacteria do not communicate to the organic compounds contained in the juices the same kinds of chemical motion as the tissue-cells. They will not, therefore, give rise to the same chemical changes as the latter. More or less serious disturbance of the normal metabolism of the tissues must ensue.

This is the first effect, but not the only one. Different kinds of fermentation cannot go on in presence of each other for any length of time. One is more and more repressed, and at length suppressed, as the other advances. This cannot, of course, happen without simultaneous injury to the corresponding ferment. Thus the prolonged presence of bacteria results in the suppression not alone of the nutritive activity, but also of the other functions of the tissue-cells; and at length their life itself is enfeebled or extinguished.

The products of the decomposition set up by the bacteria, the unorganized ferments and other poisons, also give rise to changes in the tissue-cells. It is possible that in many cases they only tend to modify the nutritive activity, *i.e.*, the metabolism of the cells; but the other functions are doubtless often affected likewise. These modifications of the normal cell-life in their totality are manifested as disturbances of the functions of the organism, and we speak of them as symptoms of disease.

The mode in which the several symptoms are produced we cannot here stop to discuss. All we need say is that a disturbance of cellular activity is always at the bottom of a morbid symptom; mere alteration in an organic fluid is not enough to give rise to symptoms. Thus the origin of fever cannot be explained otherwise than by assuming the existence of some cellular disturbance. The chief factor in producing the elevation of temperature may be a change in the fermentive action of the cells, or it may be a disturbance of the functions of the central nervous system. That is a question which is open to discussion; but it does not touch the question of the cellular nature of the febrile process.

Inflammation itself is only to be explained by cellular change. In bacterial affections, inflammation appears as a specially beneficent pro-

cess. By it a number of living cells are thrown out at the seat of danger, and they are the readiest instruments for checking the harmful influence of the fungi.

The issue of a bacterial affection is either the death of the patient, or the death and elimination of the bacteria. In the former case the bacteria interfere with the functions of cells so numerous or so essential to life, that life becomes impossible. In the latter case the tissue-cells gain the upper hand in the struggle for nourishment and existence, and the bacteria are at length deprived of the conditions essential to their continued life.

Observations on the infective diseases of man, and on experimentally produced bacterial diseases in animals, have shown that a disease of the kind successfully withstood leaves the tissues in a peculiarly unsusceptible condition. This condition may endure for months or years, and it insures an immunity almost or quite complete against a fresh invasion of the same or kindred bacteria. We do not know whether this singular effect is due to a modification in the chemical constitution of the tissues, or to a change in the vital activity of the cells.

[References: Voit, "Physiologie des Stoffwechsels," Leipzig, 1881; Nägeli, "Die niederen Pilze," Munich, 1877, and 1882; Buchner, "Die Nägeli'sche Theorie der Infectionskrankheiten," Leipzig, 1878; Klebs, Article "Ansteckende Krankheiten," "Realencyclopädie der gesammten Heilkunde von Eulenburg," and "Cellular-pathologie und Infectionskrankheiten," "Tageblatt der Naturforscherversammlung in Kassel," 1878; Virchow, "Krankheitswesen und Krankheitsursachen," "Virch. Arch.," vol. lxxix.; Hiller, "Die Lehre von der Fäulniss," Berlin, 1879; Wernich, "Die Entwickelung der organisirten Krankheitsgifte," Berlin, 1880; Koch, "Untersuchungen über Wundinfectionskrankheiten," Leipzig, 1878, "Traumatic Infective Diseases," London, 1880; Wolff, "Zur Bacterienlehre bei accidentellen Wundkrankheiten," "Virch. Arch.," vol. lxxxi.; Toussaint, "Comptes Rendus," nos. 2 and 5, vol. xci.; Chauveau, *ibid.*, no. 16; Duclaux, "Ferments et Maladies," Paris, 1882; Brieger, "Einige Beziehungen der Fäulnissproducte zu Krankheiten," "Zeitsch. f. klin. Med.," iii.; Buchner, "Ueber d. Wirkung d. Spaltpilze im lebend. Körper," "Zur Aetiol. d. Infectionskr.," Munich, 1881; Cheyne, "Antiseptic Surgery," London, 1882; Discussion, "Trans. International Med. Congr.," vol. i., 1881.

Of late years many experimenters have sought to furnish an experimental basis for the doctrine that individuals who have passed through an infective disorder are "protected" against the same or a kindred disorder (as in the case of vaccinia and variola). They have attempted to make out that this holds for bacterial disease artificially communicated to animals.

Pasteur was the first to make communications on this head ("Gaz. méd. de Paris," no. 18, 1880). Toussaint refers the so-called fowl-cholera

to the action of a certain micrococcus. Fowls die when inoculated with the bacteria cultivated in chicken-broth. If the poison be attenuated by letting it stay in the culture-liquid exposed to the air for eight or ten months, it is no longer fatal on inoculation ; but the fowls become by one or more inoculations "protected" against the unattenuated poison. Pasteur further discovered that the activity of the anthrax-bacillus may be diminished by cultivation at a temperature of 42° to 43° C. Animals inoculated with the cultivated bacillus do not die, but are as it were "vaccinated" against the unmitigated poison. After repeated inoculations sheep become at last quite unaffected by inoculation with the unaltered bacillus.

Bouley communicated to the Paris Academy a research of Toussaint's, in which he found that the anthrax-poison can be mitigated by warming infected blood to 55° C. for ten minutes with the addition of one per cent. of carbolic acid. Young dogs, sheep, horses, and rabbits may be protected by inoculation with this blood. Colin (Paris Academy, March 1, 1881) has disputed the force of these experiments, as it is known that some individual animals are specially "refractory" with respect to the anthrax-poison, without any protective inoculation. The Royal Hungarian Ministry of Agriculture instituted at Buda-Pesth an extensive series of experiments, superintended by one of Pasteur's assistants, and the results obtained confirmed on the whole what Pasteur had announced (Rószahegyi, "Biolog. Centralb.," 5, 1882, and *Practitioner*, February and March, 1882). Similar successful experiments were made in Berlin in April, 1882 ("Gaz. méd.," July, 1882). Oemler ("Arch. f. wiss. und pract. Thierheilk.," 1876–81) made similar inoculation-experiments without reaching any positive results. Chauveau likewise experimented on sheep, but was not able to draw any certain inferences ; he thinks, however, that an imperfect protection may be obtained by repeated inoculation. Löffler ("Mitth. a. d. k. Gesundheitsamte," Berlin, 1881) experimented on mice, rats, guinea-pigs, and rabbits, but was not able to verify Pasteur's and Toussaint's statements. He did not succeed either in attenuating the poison or in effectively "vaccinating" the animals. He therefore disputes the force of their experiments, thinking that they must have lighted on sheep already immune against the poison. The experiments on fowl-cholera he thinks trustworthy. It was he who showed that when a mouse has lived through one attack of specific septicæmia it is protected against a further attack.

This specific septicæmia of the mouse is caused by a delicate bacillus, which can be "purely" cultivated in nutritive gelatine, weakly alkalized with sodium phosphate and impregnated with one per cent. of peptone. The bacillus will infallibly kill a rabbit injected with it in from forty to seventy-two hours. If it be introduced into the tip of the ear it merely produces a plastic inflammation of the skin, and the animal does not die. Rabbits so inoculated are then protected for three or four weeks against any further inoculation with the same bacillus.

There are, therefore, some bacterial diseases in which one attack protects against a subsequent one, as in the case of small-pox, measles, and scarlatina. But this does not hold true of all bacterial diseases. Koch and Carter found that a monkey inoculated with the spirilla of relapsing fever gained no immunity against a second inoculation. Semmer ("Centralb. f. med. Wiss.," 48, 1880, and "Virch. Arch.," vol. lxxxiii.) asserts that rabbits may be protected against septicæmia by vaccination with bacteria heated to 55° C. for fifteen minutes; Löffler repeated the experiments and obtained opposite results. Experiments with the ***Bacillus œdematis*** (Art. 206) were likewise negative.

Bergmann has recently ("Chirurgencongress," 1882) made out that in all infective disease, and in all intoxication with unorganized ferments, the white blood-cells become dissolved in the blood. This produces greater viscidity and coagulability of the plasma. He refers to this cause the local congestions in the capillaries of the lungs and intestine, and the ecchymoses of the serous membranes observed in the affections named.]

202. The **infective diseases** form a group distinguished by their markedly specific character and their special mode of origin. The specific character is manifested in this—that the disease runs a similar course in each individual attacked, conditioned solely by the nature of the morbific virus. As to the genesis of the disease, it is always referable to the passage into the organism of a poison from without.

The infective diseases have been divided into miasmatic, contagious, and miasmo-contagious. In **miasmatic** disease the morbific virus is confined to certain localities, and develops outside the human body. When it passes into the body it sets up an affection which is not transmissible to other individuals. The malarious or intermittent fevers are classed as miasmatic.

In **contagious** disease the seat of the virus is in the affected organism. From this it is transmissible to others, either through the air directly, or by means of bodies acting as carriers (*fomites*), or by actual contact. Instances of contagious disease are scarlatina, small-pox, measles, vaccinia, typhus, diphtheria, glanders, syphilis, etc.

In **miasmo-contagious** disease the actual virus is derived from without, but the germs from which the virus develops must be furnished by a previous case of the disease. Of this kind are cholera, dysentery, yellow fever, and typhoid. In the case of the last it is probable, or at least possible, that the virus may be also derived from previously uninfected localities; in other words, that it may originate as a pure miasm.

203. Some of these diseases, especially the epidemic pestilences or plagues, have from ancient times been suspected to be due to organized poisons. The suspicion has now and again been re-expressed; but it is only within the last twenty years that, in a few instances at least, the fact has been demonstrated.

The strongest point of evidence in favor of the organic nature of the poisons that produce the infective diseases is their power of unlimited reproduction and multiplication. Thus, starting with the lymph from a single vaccine vesicle, we can vaccinate on indefinitely, continually generating new vaccine matter. Infection transmitted through the medium of the air (which certainly takes place), is scarcely to be explained if it be not that the air has had corpuscular particles suspended in it. Chemically active gases would very quickly become diffused through the atmosphere, and at short distances would become attenuated beyond the power of doing mischief.

The small quantity of infective matter required to set up the corresponding disease is another point in the evidence. The extraordinary potency of the matter can only be explained by the theory that the virus is reproduced and multiplied within the organism.

The researches of the last ten years have shown (as we have said in Arts. 198–201) that there are bacterial fungi which are able, by virtue of their specific properties, to affect the animal body and generate disease in it. On the other hand, we find such fungi in the blood and tissues of persons affected with infective disease. We must admit beforehand that the available observations on this head have not the extent or exactness which we could desire. Only in the case of a few diseases is the bacterial nature of the virus demonstrated by indefeasible histological and experimental investigation. In others the presence of bacteria has been demonstrated in single cases, but their causal relation to the disease has not been proved. In many others, neither the one point nor the other has hitherto been made out. As the question at present stands, then, we can only say—that among the infective diseases there are certainly some which are due to the invasion of a microphyte, and that it is highly probable the others have a like origin.

If the microparasitic theory be correct, we must admit that some of the pathogenous bacteria are accustomed to develop and multiply without the body, while others only do so within it. The former kind we may describe as **ectogenous**, the latter as **endogenous**. The distinction must not, however, be over much insisted on. Sometimes the ectogenous bacteria proceed to multiply within the body, while the endogenous bacteria may meet with the necessary conditions for their growth (warmth and nutriment) outside it.

[The fact that bacteria have not been found in most of the infective diseases, at least in number sufficient to account at all for the phenomena, is no proof that the affections are non-bacterial. It must not be forgotten that the demonstration of bacteria is often a very difficult matter, and the material obtained from the post-mortem table is by no means well-fitted for this purpose. The patients examined generally live on to a comparatively advanced stage of the disease. We know indeed in the case of many bacterial affections that, by the time the tissue-changes oc-

casioned by the invasion are complete, all trace of bacteria has long disappeared.]

204. The **micrococci** are among the most important of the pathogenous bacteria. They are the fungi most frequently found in connection with infective disease. In the first place they occur in various wound-affections, such as pyæmia, and erysipelas simple or phlegmonous ; and that not merely in the wound itself, but in its neighborhood, and even in distant organs. In this last case they are diffused through the lymphatics and blood-vessels. They also occur in internal suppurations like metritis, puerperal peritonitis, infective osteomyelitis and periostitis, and in strumous inflammations, meningitis, cerebral abscess, etc.

Among infective diseases of another kind we have to mention diphtheria, small-pox, measles, vaccinia, scarlatina, endocarditis, pyelitis, hæmophilia neonatorum, acute atrophy of the liver, croupous pneumonia, gonorrhœa, etc. In all of these micrococci have been seen scattered through the tissues, partly as masses of zooglœa, partly as chains or chaplets. It would seem as if in some diseases zooglœa, in others chaplets or swarms, were chiefly formed. The spherules are of various sizes ; but this character of size is not enough to enable us to distinguish between specific forms. We have as yet but few results of culture-experiments on these bodies, so that their life-history is little known. The micrococci are therefore distinguished merely by the disease to which they are related, and so we speak of *Micrococcus septicus*, *erysipelatis*, *variolæ*, *diphtheriticus*, etc.

The part played by these micrococci (which are not found in every case) is by no means certainly determined. Of some we can only say that they are frequently or always found in connection with the corresponding disease (small-pox, scarlatina, measles, hæmophilia neonatorum). Of others (as in wound-infections) we know, by experimental investigations, that they are only able to attack the tissues when they find in the system poisonous products of tissue-necrosis, or of fermentive decomposition set up by bacteria like themselves. Of many (such as those found in simple and phlegmonous erysipelas) we have every ground for believing that they can develop in the system without any special auxiliary conditions (other than slight traumatic injury).

[We shall here consider briefly the evidence for the bacterial nature of some of the infective diseases.

(1) *Purulent Inflammations ; Cellulitis ; Purulent Catarrh.*

There can be no doubt that micrococci are the exciting causes in many inflammatory processes associated with the formation of pus. This is true not only of purulent affections of the skin and mucous membranes, but also of suppurations in the deeper structures of the body.

Many of these affections start in wounds, but in others it is impossible to make out any surface-injury, and we are constrained to admit that the micrococci have penetrated into the deeper tissues without entering through a wound. Purulent catarrh of the mucous membranes, when due to fungi at all, is generally excited by micrococci from without; but these may sometimes come from deeper organs already affected, as when the urinary tract is infected from the kidney. This also holds for phlegmonous or parenchymatous inflammations of the subcutaneous and submucous structures (cellulitis), associated with purulent, serous, or fibrinous exudations. In the case of deep-seated organs, the micrococci must be conveyed by the lymphatics or blood-vessels. If by the blood-vessels, the affection should perhaps be described as pyæmic.

When the micrococci lie in the blood-vessels, they generally form colonies. In liquid exudations within the body-cavities they are found single or in chains; in solid structures they form swarms. In all places they occur both free and enclosed in cells.

It is a question whether in all the affections just cited the micrococcus met with is of the same species. Comparative examinations show that in the different cases the spherules vary in size. Ziegler found that the largest of all occurred in a case of spontaneous cellulitis of the face and neck, in which suppurating and hemorrhagic patches were found in the lungs.

References: Klebs, "Handb. d. path. Anat.," i. (pyelitis), "Beiträge zur path. Anat. d. Schusswunden," Leipzig, 1872, and "Arbeiten a. d. path. Inst.," Berne, 1872 (pyæmia); von Recklinghausen, "Verh. d. Würzburger physic. Gesell.," 1871 (pyæmic foci); Rindfleisch, "Lehrb. d. path. Gewebelehre," first edition (pyæmia); Birch-Hirschfeld, "Unters. üb. Pyämie," Leipzig, 1873; Koch, "Wundinfectionskrankheiten," Leipzig, 1878, "Traumatic Inf. Diseases" (Sydenham Soc.), 1880; Wolff, "Virch. Arch.," vol. lxxxi.; Lücke, "Deutsche Zeitsch. f. Chir.," iv.; Braidwood and Vacher, *Brit. Med. Journ.*, 1, 1882, with a very full summary of the contributions to this subject; Kocher, "Arch. f. klin. Chir.," xxiii. (osteomyelitis, infective periostitis, strumous inflammation); Greenfield, etc., "Trans. Path. Soc.," 1879; Haab, "Corresp. f. schweiz. Aerzte," 1881 (blennorrhœa, gonorrhoica neonatorum, gonorrhœa); Neisser, "Centralb. f. med. Wiss.," 28, 1879 (gonorrhœa); Cheyne, *Brit. Med. Journ.*, 1880 (gonorrhœa); Perls, "Lehrb. d. allg. Path.," ii.; Ogston, *Brit. Med. Journ.*, 1, 1881; and under Art. 199.

(2) *Erysipelas.*

Ziegler has satisfied himself by his own researches that erysipelas is due to a micrococcus. It spreads chiefly by way of the lymphatics, which are sometimes seen to be crammed full of aggregated masses of spherules. Thence it penetrates into the tissues and forms chains or swarms. It excites inflammation and leads to tissue-necrosis. It can be

transmitted to the rabbit, and spreads in it also by way of the lymphatics. The animal usually dies.

References: Nepveu, "Gaz. méd. de Paris," 1872; Lukkomsky, "Virch. Arch.," vol. lx.; Orth, "Arch. f. exp. Path.," i.; Klebs, "Arch. f. exp. Path.," iv.; Tillmanns, "Arch. f. klin. Chir.," xxiii.; Fehleisen, "Deutsche Zeitsch. f. Chir.," xvi.; Koch, "Traum. Inf. Diseases," 1880.

(3) *Septicæmia.*

This is a term which includes various rapid and fatal affections of the blood. Septicæmia in the human subject implies blood-poisoning with various chemical products of septic decomposition. It is a septic intoxication, but actual bacteria are not found in the blood. It is not progressive, and not infective in the strict sense of the word (Burdon Sanderson, *Brit. Med. Journ.*, 1, 1877). But the term is also applied by some to certain specific and infective affections of animals, in which bacteria grow and multiply in the blood itself.

Davaine's septicæmia is an infective disease of rabbits, produced by subcutaneous injection of septic matters (such as putrefying blood). It is characterized by a definite incubation-period, and a rapid course; it is transmissible to other animals of the same species. The blood is found to contain numerous oval bacteria.

Pasteur's septicæmia has been called by Koch malignant œdema ("Acad. de méd.," February 1 and 8, 1881). It is produced in rabbits by inserting garden-mould under the skin of the abdomen. Death ensues in twenty-four to forty-eight hours. The blood itself seems to contain no organisms; but subcutaneous œdema results, and in the œdematous tissues a delicate motile bacillus is found. Gaffky has cultivated the bacillus on slices of potato.

Mouse-septicæmia (Koch) is a blood-affection generated in mice by inoculation with a certain delicate bacillus. The injection of human saliva produces in rabbits a form of septicæmia not, as it seems, identical with that of Davaine (Raynaud, Pasteur). Gaffky produced still another form of septicæmia in rabbits by injecting river-water (from the river Panke). The bacteria which developed and multiplied in the blood resembled *B. termo* (Art. 205).

References: Davaine, "Acad. de méd.," September 17, 1872; Coze and Feltz, "Rech. exp. sur la présence des infusoires dans les maladies infect.," Strasburg, 1866; Semmer, "Virch. Arch.," vol. lxxxiii.; Koch, "Wundinfectionskr.," Leipzig, 1878, "Traum. Inf. Dis." (Sydenham Society, 1880); Gaffky, "Mitth. a. d. k. Gesundheitsamte," Berlin, 1881; Raynaud, "Acad. de méd.," February 8, 1881; Ewart, "Proc. Roy. Soc.," xxxii.; Tizzoni, "Arch. per le scienze," 1880–81; Sternberg, "Rep. of Nat. Board of Health (U. S.)," 1881; Braidwood and Vacher, *Brit. Med. Journ.*, 1, 1882 (a full list of contributions to the subject of pyæmia and septicæmia is given).

(4) *Diphtheria.*

This is a specific infective disease. The anatomical changes are usually first discerned in the pharynx and in the neighboring mucous membranes. They take the form of catarrhal, croupous, and diphtheritic inflammations (Arts. 423–426). They are probably caused by a micrococcus which settles in the tissues of the parts named (rarely elsewhere—as in the eye, or in wounds), and thence spreads through the system. This view is chiefly supported by the fact—that in and upon the affected mucous membranes we find micrococci scattered or aggregated as zooglœa, which do not occur under normal conditions. Occasionally it is possible to demonstrate the presence of micrococci in the swollen cervical glands, or even in deeper organs. If these micrococci be experimentally introduced into animals, they produce a disease resembling diphtheria. The micrococci multiply mainly within the body, but they may also find a suitable soil for growth outside it.

The theory of the genesis of diphtheria is still defective, in spite of the many investigations that have been made. Even what we have stated above regarding it is by no means beyond question.

References: Hüter and Tommasi, "Centralb. f. med. Wiss.," 12 and 34, 1868; Oertel, "Arch. f. klin. Med.," viii., "Ziemssen's Cyclopædia," vol. ii., "Die Aetiol. d. Diphtherie, Zur Aetiol. d. Infectionskr.," Munich, 1881; Trendelenburg, "Arch. f. klin. Chir.," x.; Klebs, "Arch. f. exp. Path.," iv., Art. "Diphtheritis," "Realencyclop. d. ges. Heilk.;" Letzerich, "Virch. Arch.," vol. lxviii.; Nassiloff, "Virch. Arch.," vol. l.; Eberth, "Zur Kenntniss d. bacter. Mycosen," 1872; Wood and Formad, "Rep. of Nat. Board of Health (U. S.)," 1881–82.

Brieger ("Zeitsch. f. klin. Med.," iii.) has lately pointed out the fact that in pyæmia, erysipelas, diphtheria, and scarlatina, certain processes take place in the tissues nearly allied to those in bacterial putrefaction. He therefore calls the diseases in question putrefactive diseases.

(5) *Scarlatina and Measles.*

We have no certain knowledge as to the causation of scarlatina. Coze and Feltz ("Malad. infect.," 1872) and Riess ("Reichert's Arch.," 1872) have seen micrococci in the blood, and by inoculation have generated a fever-like disease in rabbits. Coze and Feltz also found micrococci in the blood of patients affected with measles; Keating (*Philadelphia Med. Times*, August 12, 1882) recently found them in an epidemic of malignant measles; Ransome, and Braidwood and Vacher (*Brit. Med. Journ.*, January 21, 1882) found them in the breath as well as in the tissues.

(6) *Endocarditis.*

In many forms of endocarditis the affected patches are covered with an abundant layer of micrococci. These are also found in metastatic patches if there be any. It is very probable that endocarditis may be set up by various causes, and, as it would seem, by various forms of micrococcus (Art. 282).

References: R. Maier, "Virch. Arch.," vol. lxii.; Eberth, "Virch. Arch.," vol. lvii.; Klebs, "Arch. f. exp. Path.," x.; Köster, "Virch. Arch.," vol. lxxii.; Koch, "Mitth. a. d. k. Gesundh.," Berlin, 1882.

(7) *Variola and Vaccinia.*

In both affections micrococci have been found in the vesicles. As to their real significance nothing certain is known.

References: Keber, "Virch. Arch.," xlii.; Zülzer, "Berl. klin. Woch.," li., 1872; Weigert, "Anat. Beitr. z. Lehre v. d. Pocken," 1874; Klebs, "Arch. f. exp. Path.," x.

(8) *Hæmophilia Neonatorum.*

Klebs ("Arch. f. exp. Path.," iv.) and Eppinger ("Beiträge zur path. Anat. v. Klebs," 1878) have described a micrococcus in this disease, and have given it the name of *Monas hæmorrhagicum.*

(9) *Acute Yellow Atrophy of the Liver.*

Klebs, Waldeyer, and Eppinger ("Prag. Viertelj.," 1875) have published papers on the micrococcus found in this disease.

(10) *Croupous Pneumonia.*

Klebs ("Arch. f. exp. Path.," iv.), Koch ("Mitth. a. d. k. Gesundh.," Berlin, 1881), and Friedländer ("Virch. Arch.," vol. lxxxvii.) have seen micrococci in cases of this disease.

(11) *Acute Catarrhal Pneumonia.*

Micrococci are very often found in the alveoli and lung-tissue. They probably reach the lungs with other bacteria from the mouth-cavity (pneumonia by aspiration).

(12) *Sarcina.*

The fungus so called occurs chiefly in the stomach, lungs, pharynx, and urine. In the lungs it has been found by Nauwerck in various pneumonic affections ("Corresp. f. schweiz. Aerzte," 1881). It is much smaller than the sarcina of the stomach. Nothing is known of its significance.

We may here refer to a disease of silkworms, which throws light on

the development of bacteria within the body. It is called *pébrine*, *gattine*, or "spotted disease." It formerly produced enormous destruction among the silkworms in silk-producing districts. Investigations made in 1853–56 showed that it was associated with the presence of a micrococcus. Nägeli called the fungus *Nosema bombycis*. Pasteur proved experimentally that these organisms produced the disease, and also showed by what means it could be averted. The micrococcus is transmitted to the eggs ; the moths are therefore isolated, and after laying their eggs are microscopically examined. If the moths are found to be diseased the eggs are destroyed. Another disease of the silkworm, *maladie de morts-blancs*, which annually causes great losses to silk-growers, is very probably a bacterial affection.

Toussaint and Pasteur have shown ("Comptes Rendus," nos. 6, 17, 18, 1880) that fowl-cholera is caused by an invasion of micrococci. The organism can be cultivated in alkalized chicken-broth, which has previously been sterilized by being raised to a temperature of 110° to 115° C.]

205. The two representatives of the class of *Microbacteria*, namely, *Bacterium termo* and *Bacterium lineola*, can only develop in dead tissues and liquids. *B. termo* is frequently found in the human body at places where necrosed tissue is accessible to the air. Putrefaction is in fact conditioned by the presence of this organism. It may become dangerous by setting free products of decomposition which excite inflammation or gangrene around the putrefactive focus, and when absorbed act poisonously on the system generally or on remote organs.

[Gaffky recently discovered a specific microbacterium ("Mitth. a. d. k. Gesundh.," Berlin, 1881) which he was able to cultivate separately in sterilized gelatine impregnated with blood-serum, and in a cold infusion of boiled beef. He found the organism in river-water much polluted with sewage. The same bacterium is occasionally found in meat-washings and blood, as putrefaction sets in. It is a short rodlet which takes up aniline dyes at its poles only, the middle remaining clear. It is very like *B. termo*. Its spores have not been observed. Rabbits inoculated with it remain unaffected for ten or twelve hours, then high fever sets in, and death in twenty hours. The blood of the infected animals contains bacteria. Guinea-pigs, white rats, cats, and dogs are not susceptible, but sparrows, canaries, and chickens are. This bacterium does not set up putrefaction when "purely" cultivated ; it is therefore distinct from *B. termo*.]

206. Of the *Desmobacteria* the typical example is the best known of all microparasites, the **Bacillus anthracis**. It is found in the blood of animals affected with anthrax or splenic fever, and it is certain that it is the sole cause of the affection. The organism can be cultivated outside the body (Art. 186), and anthrax can be produced by means of the cultivated specimens. All that is needful is to introduce the bacillus or

its spores into the blood. No auxiliary conditions, such as the formation of septic products or the presence of chemical poisons, are necessary.

The spores are the commonest medium of infection, as they are hardier than the bacillus itself. Such spores develop in the blood of animals dead of anthrax even after burial (Koch). If they are not deeply buried the spores may ultimately reach the surface of the ground. Cattle are then infected through wounds (such as scratches of the mouth caused by stubble or by insects), through the alimentary canal, or through the lungs. Death seems to result chiefly from abstraction of oxygen, and disturbance of the circulation.

In man the disease is only produced by transmission of the virus from infected animals, living or dead. In England the infection is chiefly conveyed by means of the fleeces of diseased animals to persons engaged in handling them (woolsorters' disease). Anthrax in man usually contin-

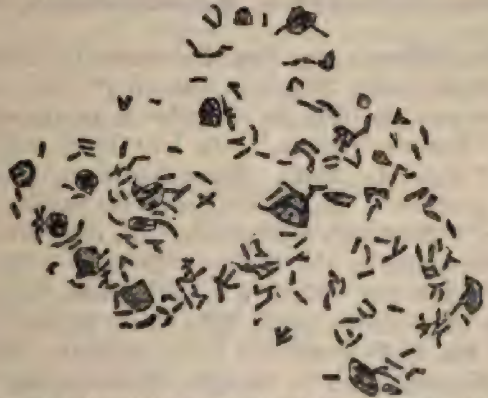

FIG. 80.—Bacillus Tuberculosis in Phthisical Sputum. × 800 circa. (Stained by Gibbes's method with magenta and methylene-blue; the pus-cells appear blue, the bacilli crimson).

ues as a local affection for a longer time than in the lower animals. Papules, vesicles, and pustules on a red and swollen base are developed in the skin. Numerous dark-red button-like nodules crammed full of bacilli then appear in the intestine. This hemorrhagic intestinal form also occurs in cattle. In human anthrax the blood usually contains much fewer bacilli than in the case of cattle.

Armauer Hansen and Neisser have lately succeeded in demonstrating the presence of a bacillus (**B. lepræ**) in the nodes and tubercles of leprosy. The constancy with which it occurs in leprous patches would indicate that it is the exciting cause of the disease (Art. 131).

Klebs and Tommasi-Crudeli have likewise found a bacillus (**B. malariæ**) in cases of malarious or intermittent fever, and have experimentally investigated its properties. They assert that it is to be met with in the soil and air of malarious districts, and can be demonstrated in the blood of affected patients. The significance of the bacillus has not, however, been fully made out.

In cases of typhoid fever Klebs and Eberth have discovered a bacillus lodging in recent infiltrations of the mesenteric and intestinal glands. Koch and Friedlaender have verified the discovery, but the life-history of the bacillus is as yet unknown.

Koch has recently made comprehensive researches into the etiology of tuberculosis. He finds that bacilli (**B. tuberculosis**) are constantly present, not merely in tubercles, but in various diffuse inflammatory infiltrations and granulomatous growths, and in the sputa of phthisical patients (Fig. 80). He is also able to cultivate the bacilli in gelatine impregnated with blood-serum, and to produce tuberculosis with striking success by inoculation with the cultivated bacilli (Art. 127). It is probable that the bacillus is unable to develop outside the animal body; and that it forms spores within the body of its host (Art. 127).

[(1) *Anthrax* (*Splenic Fever, Malignant Pustule, Charbon*).

The *Bacillus anthracis* was first discovered by Pollender in 1849 ("Casper's Viertelj.," viii., 1855) and Brauell ("Virch. Arch.," vol. xi., 1857). Davaine was the first to recognize it as the specific virus of splenic fever ("Comptes Rendus," vols. lvii. (1863) and lxxvii. (1873); "Archiv. gén.," February, 1868). Since then many investigators have examined the question of the significance of the bacillus (see Bollinger, "Splenic Fever," "Ziemssen's Cyclopædia," vol. iii.). Koch has made the most careful researches on the subject ("Beiträge z. Biol. d. Pflanzen von Cohn," ii., p. 277, and "Mitth. a. d. k. Gesundh.," Berlin, 1881), and his experiments have thrown much light on the biology of the bacillus. Toussaint also has lately published some elaborate researches ("Recherches expérimentales sur la maladie charbonneuse," Paris, 1879). Spear and Greenfield have investigated anthrax in man as it occurs in the form of "Woolsorters' Disease" ("Med. Off. Report to Local Gov. Board" for 1880).

The life-history of the anthrax-bacillus has already been given in Art. 186. It can only develop at a temperature over 18° C. and in presence of a free supply of oxygen. Hence no spores are found in the bodies of animals buried more than a metre deep. Spores may, however, very readily be produced, if in burying the animal its blood or secretions (such as urine) be allowed to contaminate the superficial soil; in summer the temperature there may rise above 18° C. (Koch).

Pasteur ("Bulletin de l'acad. de méd.," xxviii., 1880) thought that earthworms might carry spores from buried beasts to the surface, and eject them with their excreta. But Koch regards this hypothesis as unlikely and unnecessary to explain the spread of the disease. The contamination of the surface-layers in the process of burial is enough. Koch's experiments show that the transmission of the spores through the bodies of worms does not play the important part assigned it by Pasteur, but they do not exclude it altogether. Other experiments prove that

the bacillus may be cultivated on potatoes, in alkaline or neutral hay or pea-straw infusions, on crushed oats or barley, on turnip-juice, maize, beans, lentils, and many varieties of dead vegetable matter, if only sufficient water be provided. It is therefore probable that they may normally grow and develop outside the body of an animal. This takes place most readily in marshy spots and river-banks (Koch). Spores are formed in summer, and persist through the winter. Inundations then carry the germs into the pasture-lands. If Koch's views are correct, the invasion of the animal body by the bacillus is as it were an accidental incursion of an ectogenous organism. Pasteur has shown that birds enjoy no immunity against anthrax.

(2) "*Symptomatic*" *Anthrax* (*Rauschbrand*).

This disease is probably due to a bacillus found in the affected animals. It is shorter and thicker than the anthrax-bacillus, forms local aggregations in the tissues, and is accompanied by the development of gas. See Koch (*loc. cit.*), and Arloing, Cornevin, and Thomas on "Charbon symptomatique" ("Paris Acad.," June, 1881).

(3) *Malignant Œdema.*

Koch has occasionally found in putrefying matters a bacillus which produces in animals an affection resembling anthrax. He describes the affection as malignant œdema, and the bacillus as *B. œdematis.* It is fatal to mice and guinea-pigs. The site of inoculation becomes œdematous, and is beset with bacilli. These spread into the serous cavities, but except in mice the blood remains free of them. If mice be inoculated at the tip of the ear, they survive. The bacilli are somewhat narrower than anthrax-bacilli. It is possible that the bacilli found in certain affections due to poisonous meat (Huber, "Arch. f. klin. Med.," xxv.) are œdema-bacilli.

(4) *Intestinal Mycosis.*

This is a term which includes several bacterial affections. Sometimes the affection is due to anthrax-bacilli, sometimes to œdema-bacilli. It is possible that other bacilli and micrococci (Art. 477) may give rise to similar disorders.

References: E. Wagner, "Arch. d. Heilk.," xv.; Leube and Müller, "Arch. f. klin. Med.," xii.; Bollinger, "Beiträge zur vergl. Path. d. Hausthiere," Munich, 1872; Buhl, "Zeitsch. f. Biol.," vi.; Waldeyer, "Virch. Arch.," vol. lii.; Fischl, "Arch. f. exp. Path.," xvi.

Many instances of so-called "meat-poisoning" are to be reckoned as cases of intestinal mycosis. They are very probably produced by various micro-organisms and their products. In some cases the poisoning is simply septic (Art. 204 (3)); in others it is apparently specific, and in

some of these latter bacilli are certainly concerned. Exact investigations on the subject are still to be desired.

References: Zangger, "Arch. f. Thierheilk.," xxiv., 1871; Albrecht, "Wochensch. f. Thierheilk.," 1878; Kussmaul, "Arch. f. klin. Med.," iv.; Huber, "Arch. d. Heilk.," xix.; Walder, "Berl. klin. Woch.," 1878; Wyss, "Corresp. f. schweiz. Aerzte," 1881; Bollinger, "Zur Aetiol. d. Infect.," Munich, 1881; Ballard and Klein, "Report of Med. Off. of Local Govt. Board," 1880.

(5) *Syphilis.*

Klebs has a paper on a bacillus connected with syphilis in the "Arch. f. exp. Path.," x. He found microscopic rods and spherules in indurated chancres. From these he obtained bacilli by cultivation. Inoculating a monkey with these, he produced an inflammatory affection in some respects resembling syphilis, in other respects resembling tuberculosis. Ziegler made many similar experiments, but was unable to corroborate Klebs's statements. In 1878 he and von Rinecker attempted to cultivate the substance removed with all care from indurated buboes, the attempt was repeated many times, but always with negative results. Various nutritive substances were used in the cultivation-experiments. See also Aufrecht, "Cent. f. med. Wiss.," 13, 1881; Birch-Hirschfeld, *ibid.*, 44, 1882.

(6) *Malaria.*

The *Bacillus malariæ* was taken by Klebs and Tommasi-Crudeli from the air over the Italian marshes by means of a special apparatus. Its properties were tested by culture and inoculation. They also found the fungus in samples of soil taken from the same districts. They conclude—that malarious disease can be reproduced in rabbits; that it is caused by an organism; that this is present in the soil of the malarious district before it produces fever in man; and that its passage into the air can be observed under favorable conditions. Marchiafava found the bacillus in the blood, marrow, and spleen of patients who had died of malarious fever.

The *Bacillus malariæ* is an aërobious organism, which flourishes in soils of various kinds and may occur in places that are not marshy. It forms spores, and for its development requires a temperature of 20° C. Laveran found "*filaments mobiles*" in the blood of ague-patients.

References: Klebs and Tommasi-Crudeli, "Arch. f. exp. Path.," xi.; Ceci, *ibidem*, xv.; Tommasi-Crudeli, "La Malaria de Rome," Paris, 1881, "Nuovi studj sulla natura della Malaria," Rome, 1881, "Malaria and the Ancient Drainage of the Roman Hills," *Practitioner*, 2, 1881, "Istituzioni di anat. pat.," vol. i., Turin, 1882; Marchiafava and Cuboni, "Nuovi studj sulla natura della Malaria," "Acad. dei Lincei," January 2, 1881; Marchand, "Virch. Arch.," vol. lxxxviii.; Laveran, "Nature parasitaire des accidents d'impaludisme," Paris, 1881; Richard, "Comptes Rendus," 1881; Sternberg, "Rep. Nat. Board of Health (U. S.)," 1881.

(7) *Leprosy.*

Bacillus lepræ was found in all the leprous nodules they examined by Armauer Hansen ("Virch. Arch.," vol. lxxix., and *Quarterly Journ. of Micro. Sci.*, 1880) and Neisser ("Breslauer ärzt. Zeitsch.," 1879, and "Virch. Arch.," vol. lxxxiv.). The bacilli are rather longer than the semi-diameter of a red blood-cell; they lie partly within and partly without the cells of the leprous nodules. Neisser cultivated them in blood-serum and extract of meat, and observed them develop into filaments. They form spherical spores which are seated at the ends of the rodlets, or form bright vacuoles in the middle of them. They spread through the system by way of the lymphatics, not of the blood-vessels. They are surrounded by a gelatinous envelope and at times seem to be motile. Cornil and Suchard ("Annales de Dermat.," 1881) have confirmed the statements of the first observers.

(8) *Typhoid Fever.*

Klebs ("Arch. f. exp. Path.," xii., xiii.) and Eberth ("Virch. Arch.," vol. lxxxi.) have found bacilli in the diseased patches of the intestine, and in the mesenteric glands, in cases of typhoid fever. Koch has confirmed the statement ("Mitth. a. d. k. Gesundh.," 1881). In the sloughs from the intestinal ulcers long and short bacilli have been seen, in the lymphatic glands only the short ones. The latter are found also in the vessels of various organs, especially the spleen, kidneys, and liver. They are probably the exciting cause of the disease. Maragliano has found similar bacilli in the blood of living typhoid patients ("Cent. f. med. Wiss.," 41, 1882).

The above results seem at first sight to disagree with those of Fischl and Eppinger ("Beiträge z. path. Anat.," ii., Prague, 1880), Letzerich ("Arch. f. exp. Path.," ix.), and Tizzoni ("Studj di pat. sperim. sulla gen. d. tifo abdom.," Milan, 1880). These observers detected micrococci. It is possible that micrococci may settle in the typhoid ulcers by way of a secondary invasion.

(9) *Tuberculosis.*

Koch's *Bacillus tuberculosis*, mentioned already in Art. 127, grows in gelatine impregnated with blood-serum between the temperatures of 30° and 40° C., but not beyond these limits. It cannot therefore complete its development outside the body, at least in temperate climates. In most cases tuberculosis starts in the lungs, which become infected from the inspired air. The chief agent in contaminating the air is the sputum (Fig. 80) of phthisical patients, which invariably contains the specific bacillus, either with or without spores. The infective power of the sputum is not destroyed by drying. It is highly probable that the spores are likewise unaffected thereby.

The tubercle-bacilli grow very slowly, and therefore do not readily succeed in making a settlement on the surface of mucous membranes. Healthy tissues are, besides, at all times difficult to infect. The settlement is favored by wounds, loss of epithelium, stagnating secretions, etc.

The tuberculosis of domestic animals and the "pearly-disease" of cattle are due to the same bacillus as the human disease (Koch, "Berl. klin. Woch.," 15, 1882).

The bacilli grow well in sterilized ox-serum, but they develop and multiply very slowly. The colonies of fungi are only visible to the naked eye after ten days' growth; they then appear as dry whitish scales. These are made up of delicate rodlets. Each patch attains in three to four weeks the size of a poppy-seed, and then ceases to grow further until transplanted to a fresh substratum. This is owing to the fact that the bacilli have no power of locomotion, and so cannot spread over the nutrient gelatine.]

207. Of *Spirobacteria* two forms are known to occur in man. The one, apparently quite innocuous, is the *Spirochæta denticola*; it inhabits the mucous membrane of the mouth and nose. The other, the *Spirochæta* (or *Spirillum*) *Obermeyeri*, is found in the blood of patients suffering from relapsing fever, during the attacks. It is almost beyond doubt that the disease is caused by its invasion and multiplication within the blood. Quite lately the disease has been transmitted to monkeys by inoculation with the spirillum. Nothing certain is known of the habitat of the spirillum outside the body. It is easily detected by the microscope in the blood by reason of its lively movements; these sometimes cause the red blood-cells to be driven and pushed about in the field of view.

[The spirillum of relapsing fever was discovered by Obermeyer in 1873 ("Centralb. f. med. Wiss.," 10, 1873, and "Berl. klin. Woch.," 33, 1873). Since then it has often been examined and described. See Weigert, "Deutsche med. Woch.," 1876; Heydenreich, "Der Parasit des Rückfallstyphus," Berlin, 1877; Moczutkowsky, "Arch. f. klin. Med.," xxiv.; Geddes and Ewart, "Proc. Roy. Soc.," xxvii. The successful inoculation of the monkey was performed by Carter ("Deutsche med. Woch.," 16, 1879, *Lancet*, 1, 1880, and "Spirillum Fever," London, 1882).]

208. If we accept for a moment the hypothesis that all or most infective diseases (other than those due to animal parasites) are caused by the development of bacteria in some tissue or fluid of the body, we are met at once by the question whether in that case each specific form of disease has a corresponding specific bacterium. From a clinical standpoint this question must be answered in the affirmative. The most marked feature of the infective diseases is just this, that they run a typical and special course. Even though this may, in individual cases, be modified by various influences, it is in general so characteristic, so pathog-

nomonic, that the disease can often be diagnosed by its course alone. We should, therefore, have no hesitation in inferring from the specific course of the disease that the virus which excites it is also specific.

Histological examination of the tissues of patients affected with bacterial disease has shown that in some cases (relapsing fever, anthrax, tuberculosis, leprosy) well-marked forms of fungi are always detected ; and further, that these forms of fungi, or at least forms belonging to one or other of their developmental stages, are the only ones constantly found.

In other cases such histological distinction has not yet been possible. The micrococci occurring in various infective diseases do not as yet afford us characters sufficiently well-marked to form a basis for distinguishing them into species. It must not, however, be assumed that these various micrococci are identical, and that it is merely the accidental association with them of this or that poison which makes them seem to have different properties.

If the micrococcus that is found be in fact the exciting cause of the disease, we must admit that it must be endowed *ab initio* with distinct properties. From the pathological point of view as well as from the clinical, we must regard it as belonging to a distinct species. As we pointed out in Art. 183, we are compelled to classify the bacteria into species on other grounds than those that apply to the higher plants. Our classification is based as yet on their morphological and physiological peculiarities. In the case of the micrococci we are confined almost entirely to the latter. We are compelled to set up physiological species. Thus, as the chromatogenous micrococci are classified according to the color they produce, so the infective micrococci are classified into species according to their pathogenous properties.

[Koch has shown that in the case of many bacterial affections it is possible to discover in the fungi well-marked morphological differences corresponding to the physiological differences ("Traumatic Infective Diseases," 1880). Struck's papers also contain many valuable contributions of this nature. See Arts. 204–207 for further references.]

209. Each specific microparasitic disease presupposes a specific exciting cause, that is, a bacterium with special physiological properties.

In affirming this proposition we do not imply that the specific bacterium constitutes a distinct species in the biological sense. This is a question which cannot be answered by the physician ; it belongs to the biologist. He will have to make out whether the properties attributed to the bacterium are constant, and whether these properties are the only ones possessed by the corresponding biological species.

On these points observers differ widely. Koch, from his culture-experiments, has come to the conclusion that the pathogenous bacteria, like the non-pathogenous, do not alter in their properties. If bacteria be cultivated for several generations, the same developmental forms continually

recur, and their physiological properties remain in every respect the same. Even when the nutrient medium is altered from time to time no recognizable differences are produced. Koch does not dispute that mutability of species is possible among bacteria, but he holds that no adequate evidence has yet been brought to prove it.

This view has now many adherents, especially among clinical observers. Some go even further and assert that mutability of species is impossible.

The most important opponents of Koch on this point are Nägeli, Davaine, Buchner, and Wernich. Nägeli thinks that both the morphological and the physiological characters of the bacteria are mutable. A given bacillus does not invariably produce bacilli of the same structure, and does not always pass through the same developmental stages. A bacterium which under given conditions gives rise to a definite kind of fermentation, may lose this property when cultivated under different conditions (Art. 192). Thus the same fungus can set up butyric acid fermentation or lactic acid fermentation according to circumstances. Nägeli regards the various species of bacteria above described not as biological species, but as vegetative forms of a few as yet undetermined species.

[References: Nägeli, "Die niederen Pilze," Munich, 1877 and 1882; Buchner, "Die Nägeli'sche Theorie," Leipzig, 1878; Birch-Hirschfeld, "Schmidt's Jahrbücher," 1875; Wernich, "Die accommodative Züchtung der Infectionsstoffe," "Kosmos," 4, 1880; "Die Entwickelung der organisirten Krankheitsgifte," Berlin, 1880; "Desinfectionslehre," 1880; Pasteur, "De l'atténuation des virus et de leur retour à la virulence," "Comptes Rendus," vol. xcii.; Klebs, "Arch. f. exp. Path.," xiii.; Buchner, "Exp. Erzeug. d. Milzbrandbacillen aus Heubacillen," Munich, 1880; "Münchener Acad. d. Wiss.," January 12, 1882, and Nägeli's "Untersuch. üb. n. Pilze," Munich, 1882; Urlichs, "Arch. f. klin. Chir.," xxiv.; Koch, "Traumatic Inf. Dis.," 1880; "Mitth. a. d. k. Gesundh.," Berlin, 1881; Gaffky, *ibidem*: Fokker, "Virch. Arch.," vol. lxxxviii.; Wolff, "Virch. Arch.," vol. lxxxi.; Semmer, "Virch. Arch.," vol. lxxxiii.; Davaine, "Acad. de méd.," Paris, 1872; Greenfield, "Proc. Roy. Soc. Edin.," 1880, "Journ. Roy. Agric. Soc.," 1880; Klein, "Rep. Med. Off. Loc. Gov. Board," 1881; Miquel, "Bull. Soc. Botan.," 1881.

Wolff maintains that micrococci and short bacilli change into each other, and seeks to support this by showing that transitional forms exist. What he takes for transitional forms may very easily, however, be nothing more than germinating spores, or even rodlets viewed obliquely. His statement—that he obtained bacilli from a rabbit into whose peritoneal cavity he had injected micrococci—is explicable by supposing the injected matter to be impure. Wernich also asserts that the various forms may be interchanged, and speaks of the circumstance as evidence of "unstable morphological equilibrium." He gives no other evidence in support of his idea. With regard to Klebs and Billroth, and their views in this connection, see Art. 185.]

210. The defective state of our knowledge makes it for the present impossible to give a definite answer to the question of the **mutability of the bacteria.** It would, however, appear, from the researches of Nägeli and others, that we are not absolutely justified in regarding all the various forms as representing distinct biological species. The idea of a species must be based on characters that are constant, not on those which may alter with the surroundings.

The researches of Koch and his pupils do not prove that the properties of the bacteria examined by them are perfectly constant. They only show that the morphological and physiological qualities possessed by a bacterium at a given time are retained by it with some tenacity, even when a certain amount of variation takes place in its environment. On the other hand, the researches of Nägeli, Buchner, Wernich, and others seem to afford evidence that this constancy is not shown under all conditions; that changes of the nutrient medium may have some effect on the form and size of the cells, on their mode of multiplication, and on their physiological or fermentative properties. Changes of this kind and extent do not, however, indicate that one species is transformed into another. We must rather conclude that one or other of the properties possessed by a biological species of bacterium may be brought into prominence by proper modifications of the external conditions.

The mutability manifested by a given bacterium will thus have definite limits. The bacterium cannot, in any period of time within the extent of our observation, acquire properties different from any of those possessed by the species to which it belongs. As to the extent of the cycle of varieties through which any one of the known bacteria may pass, we know indeed but little. It is possible that the properties of many of them admit of only the slightest variations from those with which we are acquainted. It is, moreover, probable that many of the varieties known to us constitute true biological species.

211. If we accept the hypothesis that different vital properties of the bacteria may be brought out by different external conditions, we have next to inquire whether the pathogenous bacteria may not be peculiar varieties of non-pathogenous forms. It is conceivable that in certain circumstances a bacterial virus might be developed from an innocuous bacterium, and might ultimately be transformed back to the innocuous form again. This view has been maintained by several authors (Nägeli, Buchner, Wernich) and has been supported by various experimental results. They have chiefly relied on the observation that many bacterial poisons appear to become more virulent by transmission from animal to animal (*e.g.*, that of Davaine's septicæmia), in other words, that by continual inoculation the parasite learns to accommodate itself more and more completely to the conditions in which it is placed. The opponents of the theory of mutability diminish the force of this argument by showing that the increase of virulence corresponds with an increase in the "purity" (or freedom from admixture with other bacteria) with which

the fungus is cultivated. If a mass of mixed bacteria be injected into an animal, there will be at first several forms which develop simultaneously, and it is only after the virus has been transmitted through the living body twice or thrice that one form gets the upper hand, and develops to the exclusion of the others.

The theory of mutability, and especially that of the transformation of non-pathogenous into pathogenous forms, receives stronger support from an experiment of Buchner's, in which he seemed to show that anthrax-bacilli can be bred from hay-bacilli (*B. subtilis*) and conversely. Koch, Gaffky, and Klein dispute the validity of the experiment, but Buchner stands by it and claims to have confirmed it by fresh results of a like kind. The weight of evidence is for the present against him.

At present we are unable to draw any certain conclusion regarding the relation of non-pathogenous to pathogenous bacteria. Clinical experience would indicate that the activity of the infective virus may vary within certain limits. And we must apparently admit that the infective bacteria have not always possessed their noxious qualities, but have acquired them somehow in the course of ages. But this is not enough to convince us that harmless bacteria can acquire infective properties rapidly, that is to say, in the course of comparatively few generations. They appear rather to hold by their properties with a certain tenacity We may, therefore, provisionally conclude that the transformation of innocuous into noxious bacteria can occur but rarely and under special conditions. In other words, the pathogenous bacteria, even if they do not represent biological species, are wont to maintain the pathogenous form for long periods of time.

[Davaine, Coze, and Feltz experimented on the septic poison obtained from putrefying blood. They at first asserted that its virulence increased with extraordinary rapidity, so that in the twenty-fifth generation one-trillionth of the amount of matter originally used in the inoculation was all that was necessary to produce the same infective results. Davaine became afterward convinced that the virus attained its full power in the second or third generation. Koch confirmed this, and explained it by showing that the original matter used in the inoculation was impure, *i.e.*, contained other bacteria, and that the repeated inoculations gradually eliminated the admixture. Gaffky's experiments brought out the same result. Rosenberger ("Centralb. f. med. Wiss.," 4, 1882) has lately found that the gradual increase of virulence is more protracted in the case of the *Bacillus œdematis*.

Wernich finds that the potency of the *Micrococcus prodigiosus* (that is, its faculty of multiplying and producing red coloring-matter) can be increased by modifying the mode of cultivation. Gaffky regards this fact as likewise due to the elimination of impurities.

Buchner first announced in 1880 that hay-bacilli could be transformed into anthrax-bacilli. If hay-bacilli are injected into the blood of animals

they do not give rise to anthrax. If, however, they are bred for several generations in meat-extract and then in the arterial blood of a rabbit, they acquire noxious qualities and give rise to anthrax in mice after two to nine days' incubation. Conversely, if anthrax-bacilli are properly cultivated they can be transformed into bacilli whose properties are identical with those of hay-bacilli.

Koch (*loc. cit.*) disputes the correctness of Buchner's observations, and suggests that he has been experimenting with the œdema-bacillus (Art. 206 (3)) instead of the *Bacillus anthracis.* According to Koch the anthrax-bacillus and the hay-bacillus do not resemble each other. Hay-bacilli are rounded at the ends and possess cilia or flagella ; anthrax-bacilli are as it were cut off square. Buchner's cultures were impure, they contained germs of other bacilli, and these by degrees suppressed the original forms. While the hay-bacillus was supposed to be breeding in the blood the œdema-bacillus, or some other of similar action, was developed ; in the converse process the so-called anthrax-bacilli were gradually suppressed by others.

In a later memoir ("Akad. d. Wiss.," Munich, 1882) Buchner maintains his position and mentions fresh experiments bearing on it. In his view Cohn's *Bacillus subtilis* includes several varieties ; namely (1) hay-bacilli, (2) Pasteur's butyric acid ferment, (3) Fitz's bacterium ("Ber. deutsch. chem. Gesellsch.," ix., 1878), which converts glycerine into ethylic alcohol, (4) anthrax-bacilli. This fungus, which he regards as constituting a biological species, he calls *Bacterium subtile.* The properties of the variety which produces anthrax may be retained or withdrawn at pleasure by proper modes of cultivation. In the process of transformation transitional varieties appear representing intermediate stages between anthrax-bacilli and hay-bacilli. The middle forms only produce anthrax when injected in very large quantities. The process of transformation may be completed by cultivation in an alkaline solution of egg-yolk for twenty-four to forty-eight hours. The transformed bacillus (hay-bacillus) is distinguished by its energetic fermentative activity, and causes albumen to coagulate. It is inert when injected into the blood.

Nägeli, in his recent book entitled "Untersuchungen über niedere Pilze," (Munich, 1882), takes up the same position as Buchner with regard to the mutability of the bacteria. He believes that one and the same species may assume different forms according to the nutriment it is supplied with. These forms may exhibit different physiological and even morphological characters. The pathogenous bacteria are "nutrimental" modifications of non-pathogenous species.

Klein, in an important report just published ("Report of Medical Officer to the Local Government Board for 1881), communicates the results of a series of researches undertaken to test Buchner's hypothesis. He points out the probable sources of error in Buchner's work, and concludes that the anthrax-bacillus retains its full power to produce specific disease so long as it retains any power at all.

References : see under Arts. 209 and 219.]

CHAPTER XXXI.

HYPHOMYCETES AND BLASTOMYCETES (MOULDS AND YEASTS).

212. Mould-fungi and yeast-fungi, with their congeners, belong like the bacteria to the achlorophyllous Thallophytes. They appear to have no nearer affinity than this to the bacteria, and they have no phylogenetic relation to them. The mould-fungi and the yeast-fungi are, however, more nearly akin to each other, for it is probable that the yeast-fungi are the primitive forms from which the higher fungi have developed (Brefeld).

Moulds and yeasts, like bacteria, can only draw their nutriment from organic carbon-compounds. These they mostly find in dead organic matters, and they are therefore classed as Saprophytes. Some of them, however, are able to abstract nutriment from living tissues, and are therefore to be reckoned as Parasites. Both forms are met with in connection with the human body.

The mould-fungi or Hyphomycetes are well known outside the body. They form the familiar flocculent covering or pellicle seen on decaying organic substances, and variously known as mould, mildew, mother, etc. They belong to several distinct genera, and even to distinct sub-classes of the Thallophytes.

The yeast-fungi or Blastomycetes are also familiar organisms. They set up alcoholic fermentation, and form the yeasty scum which appears on the surface of alcoholic liquors.

[The systematic classification of the Thallophytes has, in the last year or two, undergone considerable modification.

The earlier classification, based on certain obvious characters of form and habit, was into *Algæ*, *Lichenes*, and *Fungi*. This subdivision has been modified since the disco ery of the reproductive organs, and in many cases of the entire life-history, of the various forms. No sharp line divides the algæ from the fungi. Many families of so-called algæ and fungi are really correlated, inasmuch as they agree in the characters of reproduction and "alternation." The lichens have been regarded as ascomycetous fungi, which are parasitic on particular algæ, the gonidia.

The absence of chlorophyll, and the variety of external forms (polymorphism) which occurs, are secondary characters ; the latter especially

being influenced by parasitism (Sachs, "Text-book of Botany," Oxford, 1882; Brefeld, "Botanische Untersuchungen über Schimmelpilze," Leipzig, 1874–77.)

Brefeld's classification is—(1) *Phycomycetes*=algoid fungi; (2) *Mycomycetes*=true higher fungi; (3) *Myxomycetes*=gelatinous fungi; (4) *Blastomycetes*=yeast-fungi; (5) *Schizomycetes*=bacteria.

For pathological purposes it seems more convenient to retain, as we have done, the older and well-marked classes of bacteria, moulds, and yeasts.]

The Hyphomycetes or Moulds.

213. **Morphology and physiology.** The mould-fungi are hyphomycetous, *i.e.*, they are fungi characterized by the formation of a *mycelium*. As they occur in man they appear in the form (1) of simple or branched, jointed or unjointed filaments of various thicknesses, and (2) of ovoid or spherical cells. These filaments are the *hyphæ* (Fig. 81); the compact masses or tufts which they form are *mycelia;* the spherical, ovoid, or cylindrical cells, often strung into a kind of chaplet, are the *spores*, or rather the *conidia*. Spores are more commonly found within the human body than any other of the vegetative forms; fructification is rarely observed. These fungi are classified according to the place in which they are found, and the affection which they produce. Their names are derived from the name of their discoverer, from the name of the disease they produce, or otherwise. Such a classification can only, of course, be a temporary expedient.

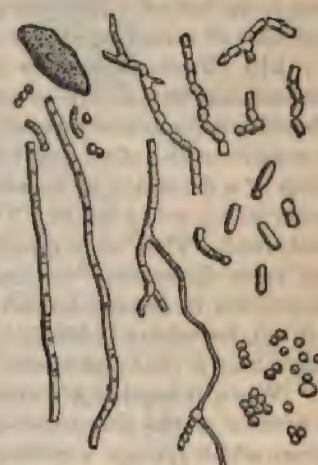

FIG. 81.—Fungi from a Favus-patch. (Neumann.)

The filaments and spores are not the plant, they represent merely a developmental stage of it, and by no means determine the species. To settle this the plant must be purely cultivated on a proper soil, and its various stages traced out.

In all cases the cell which we call the spore or conidium grows into a germinal tube or cylinder, and from it spring a greater or less number of ramifying unicellular or multicellular filaments or hyphæ. These form a mass which, taken as a whole, is called the mycelium. This again may give rise asexually to reproductive cells, which develop into fresh mycelia. In other cases sexual organs are formed, and the product of the congress of the male and female elements is either a single spore (*zygospore*) or a fructification in which numerous spores (*ascospores*) are developed. From the zygospore, or from the ascospores, the new generation

springs. The former is the case in *Mucor Mucedo;* the latter in *Aspergillus glaucus*, and *Penicillium glaucum*—the commonest of the ordinary moulds.

214. The genus *Oïdium* exhibits the processes of growth and multiplication in their simplest form. It forms a white downy covering on decaying organic substances, especially on animal excreta, fruit, grapes (*Oïdium Tuckeri*), and sour milk. According to Grawitz ("Virch. Arch.," vol. lxx.) *Oïdium lactis*, which grows upon the surface of milk, passes through the following stages of development. The conidia or spores, which are ovoid cells, lengthen out into one or more germinal tubes, which very soon become jointed and throw out lateral branches. These branches are at first cylindrical, but later on they become rounded off, and then appear as lengthened ovoids. Sooner or later they break up by transverse subdivision into chains or chaplets of conidia. The several conidia-cells then recommence the developmental cycle, which proceeds as before. No true *sporangia* or spore-capsules are formed, and no kind of sexual reproduction has been observed.

215. *Mucor Mucedo* is a mould-fungus which grows on all kinds of substances, but chiefly on excreta and on articles of food. It forms the familiar white mouldy covering. When the spores are numerous it takes on a brownish-yellow powdery look. If these spores be sown on the surface of a decoction of horse-manure, for instance, they proceed to germinate within a few hours. The long ovoid spores become larger and more spherical. Then they throw out their germinal tubes or hyphæ in one or more directions. In twenty-four hours a dense interlacing weft of mycelium is already formed, made up of non-septate filaments (Fig. 82, *B*, *m*), branching indefinitely into finer and finer expansions. The entire mycelium is thus one enormously branched cell.

When it reaches a certain point this vegetative growth ceases. The contents of the filaments become turbid, and draw toward the middle, from which springs a stouter branch than the rest, the *conidiophore* or *sporangiophore* (*g*). When this has grown somewhat, a button-like protuberance appears at its apex; this is the *sporangium*. It consists of an enclosing membrane and a protoplasmic core. The protoplasm becomes segmented, and thus are formed a multitude of conidia (*A*). Septa then begin to develop in the filaments of the mycelium.

These sporangia are non-sexual structures. When ripe they consist of a membranous spherical envelope, containing a mass of spores agglutinated by a sticky intercellular substance. In water the membrane gives way, and the conidia are set free.

The mode of multiplication just described is the commonest; but there is also a sexual mode of propagation by means of what are called *zygospores*. The process is this:—the tips of two filaments rising from the mycelium are each marked off by a septum, so that each ends in an apical cell (Fig. 82, *D*, *aa*). These tips meet and the cells coalesce, and by absorption of the separating membranes the contents flow to-

gether. The single new cell thus produced is the zygospore. Its membrane becomes thickened and it grows to a considerable size. The thickened membrane is divisible into a blackish *exosporium* and a colorless *endosporium*. From this zygospore, which in the case of *Mucor* is also a resting-spore, there springs, after some weeks of cultivation, a germinal hypha ($C\ k$), which then develops a hypha bearing a sporangium (g).

Fig. 82.—Development by Conidia and Zygospores. *A*, the conidiophore or conidia-bearing hypha of *Mucor Mucedo* in optical section; *B*, mycelium of *Phycomyces nitens*; *g*, conidiophore; *m*, unicellular mycelium (three days old; grown in plum-decoction and gelatine; the finest ramifications are left out in the drawing; from Sachs); *C*, germinating zygospore (*z*) of *Mucor Mucedo*; the germinal tube or hypha (*k*) throws out a conidiophore (*g*); *D*, free conjugating branches (*b*, *b*) whose tips (*aa*) have not yet coalesced, but are marked off by septa; the zygospore results from the coalescence of the cells (*aa*).

[We owe most of the details of our knowledge on this part of the subject to Brefeld ("Botan. Untersuch. über Schimmelpilze," Leipzig, 1874–77); the foregoing account is taken from him. The mycelium of *Phycomyces*, in the figure taken from Sachs, agrees generally with that of *Mucor*; in the latter, however, only a single conidia-bearing hypha is developed.]

216. The life-history of *Eurotium Aspergillus* (*Aspergillus glaucus*) and *Eurotium repens* is somewhat different. These two fungi are found

on various substances, but chiefly upon cooked fruit. They form a finely filamentous-jointed mycelium (Fig. 83, *A*), from which rise a great number of aërial hyphæ or conidiophores (*c*). These end in a spherical knob, from the upper part of which sprout numerous densely packed radial peg-shaped protuberances or *sterigmata* (*st*). Each sterigma gradually develops a long chain of conidia, so that the head of the conidiophore is at length covered with a sheaf of such chains.

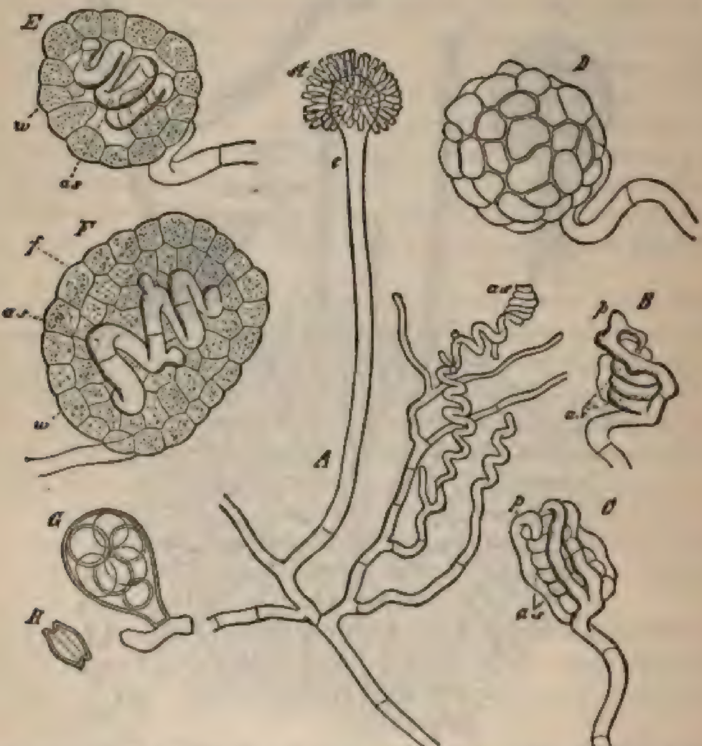

FIG. 83.—Development of *Eurotium repens*, and of *Aspergillus glaucus* (after De Bary). *A*, small part of mycelium with a conidiophore (*c*) and young carpogonium (*as*); *B*, the spiral carpogonium (*as*) and pollinodium (*p*); *C*, the same, with commencing growth of filaments to form the wall of the perithecium; *D*, a mature perithecium; *E* and *F*, young perithecia in optical section; *w*, wall-cells; *f*, "packing-cells" or pseudo-parenchyma; *as*, ascogonium; *G*, ascus; *H*, ascospore.

While the conidia are developing, the sexual organs are being formed within the same mycelium. The end of a mycelial filament becomes twisted like a corkscrew (*A as*); and the spiral turns come closer and closer to each other, till at last they touch and form a hollow spiral tube. This is the female organ or *carpogonium* (*as*). From the lowermost turns of the carpogonium thin branches sprout out, which grow up over the outside of the spiral. One of these, growing more quickly than the rest, reaches the uppermost turn and applies its point closely to it (*B p*). This is the male part or *pollinodium*. Conjugation takes place between

it and the carpogonium ; the bounding membranes give way, and the contents coalesce. Thereupon from the lower part of the pollinodium and carpogonium spring new filaments, which increase rapidly in number and cling closely to the spiral (*C*), so as at length to cover it up completely. These tubular filaments subdivide transversely, and so an envelope of polygonal cells (*D*) is finally formed. This envelope is the *perithecium*, and it forms a hollow sphere (*E w*) containing the carpogonium. The cells multiply so as to fill up the cavity (*F*). Meanwhile numerous septa are formed in the carpogonium, and from the joints spring lateral branches (*ascogenous hyphæ*), which ramify and subdivide (*F as*) between the surrounding cells. Their terminal twigs form the *asci* (*G*) (whence the fructifying carpogonium is named the *ascogonium*). The asci are tubular, and in each of them eight spheres (*ascospores*) are developed. As the ascogenous filaments develop, the "packing cells" or pseudo-parenchyma of the perithecium disappear. Ultimately the asci also vanish, and we are left with a hollow receptacle filled with spores. When ripe these last are lenticular or biconvex (*H*). On germinating they again form a mycelium, which produces both conidia and perithecia. There is no true alternation of generations between the sexual and asexual varieties.

217. The commonest of all mould-fungi, *Penicillium glaucum*, develops in a similar way. It grows on the most meagre soils. Until lately the mycelium with its conidia was the only form of it which had been recognized. Brefeld showed, however, that it is an ascomycetous fungus allied to the *Tuberaceæ* or truffles.

The mycelium consists of jointed, much-branched, uniform filaments. Some of these rise as conidiophores, which branch at the apex into sterigmata, and produce rows or chains of greenish-colored conidia. *Penicillium* may pass through several generations, all following this mode of propagation.

But there is also a sexual mode. As in *Eurotium*, a spiral female carpogonium and a male pollinodium are developed. In the former the germs of the new plants are produced.

After fructification the carpogonium throws out thin sterile filaments which interlace to form an envelope for it ; and also a thicker filament lying in the centre and constituting the germinal or sporiferous element, which takes the form of a branching tube. The densely packed enveloping filaments subdivide freely, so as to produce a compact and coherent mass of cells. The cells increase greatly in size, and their walls become firm and hard ; so that the structure appears at last as a firm ball or tuber, looking like a yellow grain of sand. This is called the *sclerotium*, and may be preserved in the dry state for many months together.

On germinating ascogenous filaments are developed within the carpogonium and grow out into threads, some of which are stout, while others are slender. The latter have to do with the absorption of nutriment from the enveloping capsular tissue, the former with the process of fruc-

tification. Clusters of asci are developed upon them, each containing eight spores. The whole of the enveloping tissue is ultimately absorbed, with the exception of the brownish outer layers. The asci and the filaments likewise vanish, and after some months we have left merely a hollow capsule filled with a multitude of bright yellow spores. From these spores or ascospores an ordinary mycelium is again reproduced.

218. The life-history of a few of the most common of the filamentous fungi, some of them occurring in the human body, exemplifies the fact that the various forms have various modes of development and reproduction. In some the process of reproduction is very simple. The mycelium gives rise by subdivision and abstriction to separate cells or conidia, which have the faculty of existing independently, and of developing a fresh mycelium. In others a second, more complex but still asexual, mode obtains ; the mycelium shoots out specially constructed conidiophores or sporangiophores, and these bear sporangia, or sterigmata. In or upon these receptacles are developed reproductive cells, which we term conidia or spores.

But there is a third or sexual mode of propagation. In this two equivalent cells unite to form a new cell—the zygospore (as in *Mucor*) or true resting-spore ; or a female organ develops—the carpogonium—which, fructified by the agency of a male organ or pollinodium, develops a germinal or ascogenous organ ; and this again, by a process of branching and subdivision, produces asci or spore-tubes containing the true spores or ascospores. From these the cycle of development may begin once more.

This sexual reproduction may either go on simultaneously with the asexual modes, or an alternation of generations may take place. That is to say, from a conidium a mycelium is developed which possesses sexual organs, and from these is sexually generated an asexual plant. This bears ascospores, and they again form a mycelium which produces conidia. It is not to be forgotten, however, that strict alternation of this kind rarely occurs. Without prejudice to the plant the alternation may be pretermitted for many successive generations, as is the case with *Penicillium*. In any case, indeed, the number of asexual generations is much greater than the number of sexual ones.

Such an alternation of sexual with asexual generations is not peculiar to the fungi ; it occurs in a much more definite manner among higher plants. No peculiar polymorphism is exhibited by the fungi. The idea of polymorphism has arisen from the fact that the asexual mode of reproduction is very common among fungi, while the sporangiophores or conidia-bearing organs assume very various forms. Moreover, in all of the fungi there is more than one mode of asexual reproduction. The statement of various authors (like Hallier)—to the effect that fungi possess a special and peculiar habit of polymorphism or "pleomorphism"—rests mainly on error. They have either failed to cultivate "purely" the plants studied, or they have been ignorant of the diverse modes in which they may be propagated.

[The account just given by no means exhausts the various modes of sexual and asexual reproduction among the fungi. We have, for example, said nothing of the formation of *oospores*. Here a female cell or *oosphere* develops in an *oogonium*, and is fructified by a male cell or *spermatozoid* developed in an *antheridium*. From this is bred a plant like the parent-plant, or else a multitude of germs which go to produce a new generation. For such details and others we must refer the student to Sach's "Text-book of Botany," or to Brefeld's papers above cited. All we have here attempted is—to give such an account as would make clear the general modes of growth and reproduction of the mould-fungi, and enable the student to understand the allusions to them that are constantly occurring in articles on the fungous parasites of man.]

219. The form and texture of the mycelium and the mode of multiplication depend greatly on the nature of the nutrient substratum. Thus the filaments of *Oïdium lactis* may be short or long, thin or thick, according to the proportion of sugar present and the reaction of the solution. If there is a dearth of nutriment, the formation of conidia is generally favored. The free access of oxygen is also of import. According to Brefeld sexual reproduction can be induced in *Penicillium* if the access of air and light is prevented after the mycelium is formed.

If spores of *Mucor* be sown in a saccharine liquid with access of air, the mycelium developed on the surface is made up of branched non-septate hyphæ, and the liquid absorbs oxygen (Reess, "Botan. Untersuch. über Alkoholgährungspilze," 1870; and Fitz, "Ber. d. deutsch. chem. Gesell.," Berlin, 1873). If the mycelium be immersed, or oxygen withdrawn, the hyphæ develop septa and break up into longer and shorter segments; these then multiply by budding like the yeast-plant, and form a kind of large-celled yeasty scum. This yeast has the power of decomposing sugar into alcohol and carbonic acid, but the fermentation ceases when a small proportion of alcohol is formed. The same is true of *Mucor racemosus*, but not of *Penicillium glaucum*.

If the composition of the nutrient substratum be gradually altered, the fungi may be got to grow on substances which they do not usually affect. Thus *Eurotium* and *Penicillium* may be transplanted from bread to solution of peptone, and can ultimately be made to grow on the surface of blood (Grawitz).

The limits of temperature, within which the mould-fungi can flourish, vary with the different forms. Some species of *Aspergillus* (*A. flavescens*, *fumigatus*, *nigrescens*) and some of *Mucor* grow very well at temperatures between 35° and 40° C.; while *A. glaucus* and *Penicillium* only thrive below 34 C°. The spores bear high degrees of heat; to kill them outright they must be kept at a temperature of 110° to 115° C. for an hour.

[References: Grohe, "Berl. klin. Woch.," 1, 1871; Löffler, "Mitth. a. d. k. Gesundh.," Berlin, 1881; Grawitz, "Virch. Arch.," vol. lxxxi.;

Lichtheim, "Berl. klin. Woch.," 9, 1882; Leber, "Gräfe's Arch.," xxv., and "Berl. klin. Woch.," 19, 1882; Duclaux, "Ferments et Maladies," Paris, 1882; Koch, "Berl. klin. Woch.," 52, 1881; Kaufmann, "Lyon médicale," 1882.]

220. The **action** of the mould-fungi **on the nutrient soil** on which they grow is slow, and limited in extent. Thus the mouldy covering which forms on preserved fruit extends only to a slight depth below the surface. Mouldy articles of food acquire a peculiar, unpleasant, "musty" taste. If the mycelium of a fungus gains access to an apple, for instance, the apple becomes rotten; *i.e.*, a process of change and decay sets in accompanied by purely chemical decompositions. Timber in which mould-fungi develop becomes soft and brittle, and breaks down into a dry "mouldering" dust. Fungi which are specifically distinct may give rise to similar or identical decompositions in articles of food, timber, etc. The mycelium of *Merulius lacrimans* (dry-rot) destroys the wood-work of houses.

Moulds may likewise attack living plants, *i.e.*, they may thrust their mycelia into living vegetable tissue. The changes they occasion are various. Sometimes they seem to exert no disturbing influence on the normal development of the tissue. In others they induce abnormal growths. The so-called "witches' brooms" of the silver fir are produced by the settlement in the tree of the *Aecidium elatinum*. Often the cell-contents become altered; thus starch and cellulose may be converted into turpentine. Hartig thinks the moulds may also act as organized ferments.

Not infrequently the fungi destroy altogether the plants they attack. Thus the *Oïdium Tuckeri* (vine-mildew) seizes on the green parts of the vine, and destroys it. If the spores of *Peronospora infestans* reach the tubers of the potato-plant, they drive their germinal hyphæ into their substance, form a mycelium there, and so ruin the potato (De Bary); this constitutes the "potato-disease." The "leaf-rust" which destroys fruit-trees is likewise due to a fungus (*Roestelia cancellata*).

[References: Sachs, "Text-book of Botany," 1882; De Bary, "Die gegenwärtig herrschende Kartoffelkrankheit," Leipzig, 1861, *Journ. of Botany*, 1876, "Botan. Zeitung," 1881; Hartig, "Ueber die durch Pilze bedingten Pflanzenkrankheiten," Munich, 1881.]

221. **Pathological significance.** The mould-fungi do not act as producers of disease to anything like the same extent as the bacteria. The fact that they require abundance of oxygen and flourish best at temperatures below that of the body hinders their development within it. Moreover, their growth and reproduction are much slower than in the case of the bacteria, and this also is a hindrance to the invasion of living tissues by them. Lastly, they do not usually find in living tissues their proper nutriment. At the same time the products of the decompositions

set up by them are by no means so poisonous as those which result from the development of bacteria. For these reasons the effect of mould-fungi or their germs on the system is either *nil*, or very limited.

Multitudes of fungus-germs are received into the accessible cavities of the body with the air, water, and food. Most of these germs fail of development and perish, or are removed from the body. It is only now and then that they produce hyphæ, and that only when they reach spots accessible to the air and containing necrotic tissues or other like matters. Such spots are the mouth, nostrils, and pharynx, and the external auditory meatus, the cornea, trachea, bronchi, and lungs. In the "fur" of the tongue of patients whose mouths are not kept clean we often find not only bacteria but also the spores and hyphæ of various filamentous fungi. In cases of bronchiectasis, vomicæ, and pulmonary gangrene various forms of mycelial growths, such as *Mucor*, *Eurotium*, and *Aspergillus*, have been frequently described. They produce hyphæ and conidia, and (rarely) the more complex conidiophores.

These fungi are not, however, to be regarded as the specific causes of the diseases in question. They are merely secondary growths developing on the dead tissues produced by antecedent morbid processes. They have merely sprung up on a soil which they found already prepared. They are not parasites, they are merely saprophytes. But their development in the necrotic matters, and the further decay they set up, may nevertheless tend to excite inflammatory action in the neighboring tissues.

The fungi found occasionally in the stomach are in like manner to be regarded as secondary formations. They are not causally connected with the disease which they accompany. They are sometimes observed in cases where the gastric functions are gravely impaired, as in carcinoma and in dilatation of the stomach. The form of vegetative growth then met with is not the ordinary one ; the fungi multiply by subdivision into short cells resembling those of the yeast-plant. This phenomenon we have already seen exemplified in the case of *Mucor* when grown under the surface of the nutrient liquid.

[On mycoses (or fungus-affections) of the lungs see Virchow, "Virch. Arch.," vol. ix. ; Küchenmeister, "Die in dem und an dem Körper des Menschen vorkommenden Parasiten ;" Friedreich, "Virch. Arch.," vol. x. ; Pagenstecher, "Virch. Arch.," vol. xi. ; Cohnheim, "Virch. Arch.," vol. xxxiii. ; Fürbringer, "Virch. Arch.," vol. lxvi. ; Lichtheim, "Berl. klin. Woch.," ix., 1882 ; Bollinger, "Zur Aetiol. d. Infect.," Munich, 1881 ; Kitt, "Deutsche Zeitsch. f. Thiermed.," vii.

The *Aspergillus* which is found in the lungs is, according to Lichtheim, the *A. fumigatus*. It was formerly believed that *A. glaucus* occurred within the body. This cannot be the case, however, for the body-temperature is too high. *A. glaucus* forms rounded conidia-spores 12–13 micromm. in diameter, with a thick, warty, yellowish envelope. Those of

A. fumigatus are only 3–4 micromm. across, and are smooth. Invasions of the *Aspergillus* are very often observed in birds.

In the external meatus and middle ear the following are found—*Aspergillus fumigatus, nigricans, flavescens*, and *Trichothecium roseum*. They excite inflammation. The instillation of oil favors their development (Bezold, "Ueber Otomycosis, Zur Aetiol. d. Infect.," Munich, 1881).

Aspergillus may grow on the injured surface of the cornea and lead to suppurative inflammation. Leber ("Gräfe's Arch.," xxv.) has cultivated it on the cornea and in the anterior chamber of rabbits. *Aspergillus* also occurs in the pelvis of the kidney.]

222. Filamentous fungi are the exciting causes of certain skin diseases. In Favus, Tinea tonsurans, Tinea versicolor, Tinea sycosis, and Onychomycosis deposits of hyphæ and conidia are found in the epithelial layers of the skin.

In Favus, for example, the root and root-sheath of the affected hair (Fig. 84, *a*, *b*) are beset with jointed filaments and spores. The other parts of the hair and skin are also interpenetrated with filaments and spores, and these tend to separate the constituent epidermoid cells by loosening their cementing substance. Inflammation is set up and scales and crusts are formed on the surface. Grawitz asserts that the hyphæ and conidia, which are met with in the above-named mycoses of the skin, all belong to the same species of fungus, which is identical with the *Oïdium lactis*; the differences observed in the various diseases being simply due to differences in the nutrient substratum. Most authors, however, maintain that they belong to different species. The fungus of Favus is called *Achorion Schönleinii*, that of Tinea tonsurans (or ringworm) is *Trichophyton tonsurans*, and that of Tinea or Pityriasis versicolor is *Microsporon furfur*.

Most of the parasitic filamentous fungi infesting man seldom penetrate beyond the superficial layers of the tissues affected. They can only do so under special and uncommon conditions, as in deep wounds. Some few, like *Aspergillus fumigatus* and *flavescens*, can germinate and throw out filaments into the blood, if they succeed in entering the vessels; but they do not multiply. As they grow they excite inflammation and necrotic changes. Only two fungi referred to this class are known to multiply in the substance of the tissues, and they cause widespread and highly destructive inflammations. One of these is the so-called *Actinomyces* or "ray-fungus" which causes the disease known as Actinomycosis (Arts. 134–135). Its botanical position is not yet determined; if it is a mycelial fungus at all, it differs in many respects from its congeners. Some pathologists go so far as to question whether it is a vegetable. The other is the *Chionyphe Carteri*, which is found in tissues affected with the Indian disease known as "madura-foot" or Mycetoma. Its mycelium penetrates the skin and subcutaneous tissue, and suppuration and ulceration are set up.

[The earliest observation of filamentous fungi in the deeper organs was made by Zenker ("Jahresb. d. Gesell. f. Natur- und Heilk.," Dresden, 1861–2). He found them in cerebral abscesses.

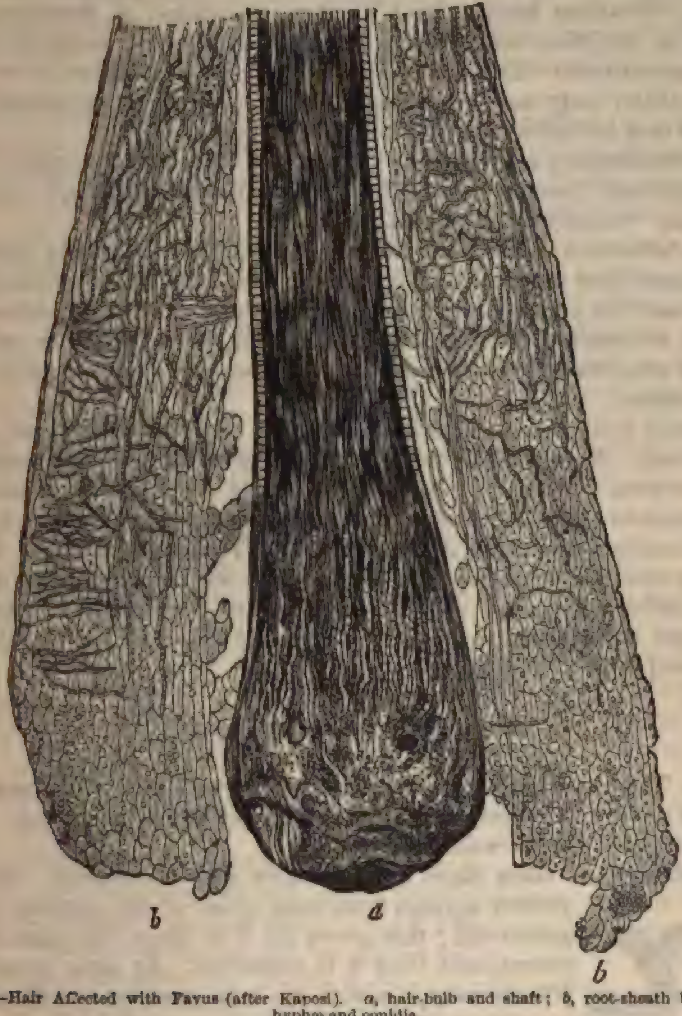

FIG. 84.—Hair Affected with Favus (after Kaposi). *a*, hair-bulb and shaft; *b*, root-sheath beset with hyphæ and conidia.

Grohe ("Berl. klin. Woch.," 1, 1870) and Block ("Ueber Pilzbildung in thier. Geweb.," In. Diss., Stettin, 1871) made the first experimental researches on the behavior of mould-spores introduced into the blood. They affirmed that the spores of *Aspergillus glaucus* and *Penicillium glaucum* germinate when injected into the blood, so that the tissues become penetrated with their filaments. Their experiments were again and again repeated, but their results were not confirmed until Grawitz took

up the subject ("Virch. Arch.," vol. lxxxi.). He found that to obtain positive results the fungi must first be adapted to the conditions of the human body by cultivation in an incubator. Koch, Löffler, and Lichtheim (Art. 219), however, showed that this is not always necessary, for the conidia of various moulds, such as *Asp. fumigatus*, *A. flavescens*, and several of the *Mucorini*, have the power of developing within the body. Experiments made with a view to acclimatize other varieties to the conditions of the body were unsuccessful. Grawitz's results are vitiated by the fact that his cultures were probably "impure."

On Madura-foot see Vandyke Carter "On Mycetoma," London, 1874, and Lewis and Cunningham, "The Fungus-Disease of India," Calcutta, 1875, and "Quain's Dict. of Med.," 1882.

The affections induced by the mould-fungi have a totally different significance from those induced by the bacteria. No transmissible infective disease has yet been produced by the former class of organisms, for they do not multiply within the body. In all the experiments referred to what was obtained was at most the germination of conidia—never their fructification.

Among invertebrate animals diseases due to mycelial fungi are by no means rare. *Botrytis bassiana* sets up the so-called muscardine-disease in silkworms. *Cordyceps militaris* destroys the noxious pine-spider (*Gastropacha pini*). *Tarichium megaspermum*, a black fungus, is fatal to the noxious caterpillar *Agrotis segetum*. The genus *Empusa* is well known; one of its species (*E. radicans*) attacks the caterpillar of the white cabbage-butterfly, another (*E. muscæ*) the ordinary house-fly. These are often found completely beset and permeated with mycelial filaments.]

The Blastomycetes or Yeasts.

223. The yeast-fungi consist of round or ovoid cells of various sizes (Fig. 85). The cell-protoplasm is granular, and often vacuolated. It is contained within a cell-wall.

Multiplication takes place by gemmation and abstriction. An outgrowth springs from some point of the surface of the parent-cell; this grows till it is about the size of the parent, and then it is abstricted. In some conditions (Cienkowsky, Grawitz) the cells grow out into filaments, but these do not become jointed or subdivided. If jointed threads seem to be formed, it is by a process of gemmation, like that which produces the rounder cells. Dilution of the nutrient liquid favors the development of filaments; abundance of sugar favors the development of spherical cells. Reess asserts that new cells may also be formed endogenously, by means of so-called brood-cells.

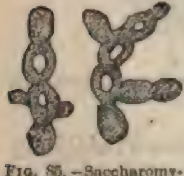

FIG. 85.—Saccharomyces Cerevisiæ. × 400.

The organism which sets up alcoholic fermentation is a yeast-fungus

(*Torula*). When it multiplies in a liquid containing sugar, alcohol and carbonic acid are generated. It has therefore been described as *Saccharomyces*. The scum which forms on the surface of alcoholic liquors and leads to their transformation into vinegar also contains a yeast-fungus; it is distinguished as *Mycoderma vini* or "mother of vinegar." Nägeli maintains that *Torula* and *Mycoderma* are not distinct species.

[Sachs classes the yeasts with the bacteria as *Protophyta*. Brefeld regards them as probably mere low forms of the moulds or filamentous fungi. Cienkowsky's paper on *Mycoderma* is in the "Mélanges biologiques de l'acad. de St. Pétersbourg," vol. viii.; Grawitz's in "Virch. Arch.," vol. lxx. On *Saccharomyces* and alcoholic fermentation see Reess, "Bot. Untersuch. üb. d. Alkoholgährungspilze," Leipzig, 1870; Pasteur, *Op. cit.* (Art. 191), "Studies on Fermentation," London, 1879; Mayer, "Lehrbuch d. Gährungschemie," 1876; Schützenberger, "Fermentation," London, 1876; Brefeld, "Phys. med. Gesellsch. zu Würzburg," v., 1873; Hiller, "Die Lehre von der Fäulniss," Berlin, 1879. On the various theories of fermentation see Art. 191.

Yeast-cells not only set up fermentation directly, but they yield an unorganized ferment which changes cane-sugar into grape-sugar.]

224. The yeast-fungi have but little pathological importance. They have no power of invading living tissue, and therefore they are only to be found in parts that are accessible from without. Even there it is only under specially favorable conditions that they are able to grow freely. There is usually no great supply of fermentable saccharine matter available for them. It is in the stomach that they are oftenest found, and there they may set up fermentation; the presence of the gastric acids does not check their development. If fermenting "wort" or "must" be drunk, the fermentation goes on in the stomach.

According to Grawitz the white patches known as "thrush" (or aphthæ) which form in the mouth, pharynx, and œsophagus of weakly children and debilitated patients are due to the presence of *Mycoderma vini*. The mycelial filaments and spores found in these patches have usually been regarded as belonging to an *Oïdium* distinguished as *O. albicans*. Grawitz has shown that on cultivation the filaments gemmate like *Torula* and *Mycoderma*. He has further proved experimentally that the latter can be grown in the epithelium of the mucous membrane. The subepithelial fibrous tissue is not usually invaded, and then only when by antecedent changes, constitutional or other, the resisting power of the tissues has been considerably diminished.

CHAPTER XXXII.

ANIMAL PARASITES.

Arthropoda.

225. **Arachnida.** The arachnoid parasites are mostly ectozoa; they inhabit the skin for a shorter or longer time. Only a single species, ***Pen-***

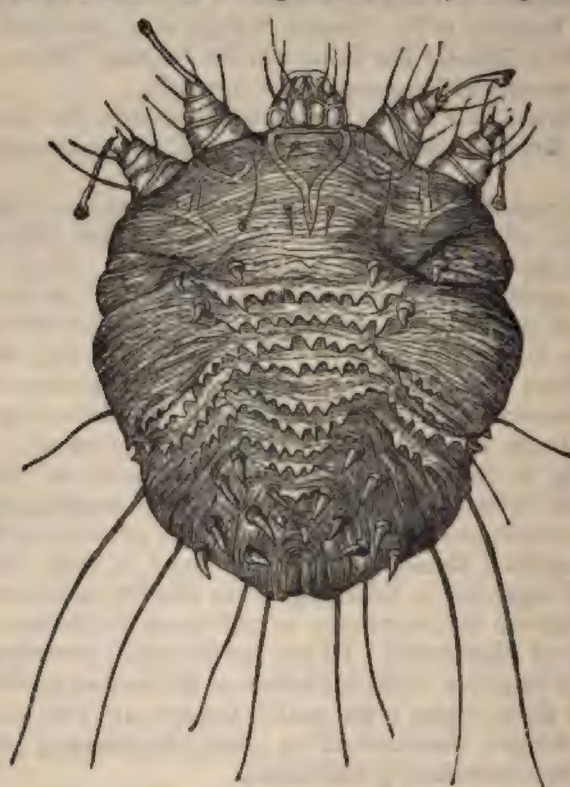

FIG. 86.—Female *Acarus Scabiei*, Dorsal Surface. × 200. (From Hebra's Atlas of Skin Diseases.)

tastoma, is found (in the larval form) within the substance of the deeper tissues.

(1) *Acarus scabiei* (*Sarcoptes hominis*), or itch insect. This mite is

about the size of a small pin-head, and somewhat turtle-shaped. It has four pairs of legs springing from the ventral surface, each being furnished with bristly hairs (Fig. 86). The anterior pairs are prolonged into stalked suckers, as are also the posterior pairs in the male. The foremost of the two posterior pairs in the male and both posterior pairs in the female end in a long bristle. The border of the body behind is likewise furnished with bristles, and the dorsal surface is beset with tooth-like hooks and spines. The head is blunt and rounded, and beset with bristles. The female is about twice the size of the male.

FIG. 87. — Acarus Folliculorum. × 300. (From Perls.)

The mite lodges in the epidermal layer of the skin, in which it excavates burrows or *cuniculi* that may run to 10 mm. in length. In these burrows the female lays her eggs. From the eggs the young acari are hatched *in loco*; they proceed to burrow further into the epidermis, and after changing their skin several times become sexually mature. The irritation caused by their presence produces inflammation of the skin. This again is greatly intensified by the scratching induced by the intolerable itching of the affected parts.

(2) *Leptus autumnalis*, or harvest-mite. This likewise infests the epidermis. It is red in color, and thus is readily seen in spite of its smallness. It gives rise to the formation of papules and wheals. Two allied American species are the *Leptus Americanus* and *L. irritans*.

(3) *Acarus* (*Demodex*) *folliculorum* (Fig. 87). A third mite, which is found solitary or in small numbers in the sebaceous matter of the follicles in perfectly healthy skin. It is about 0.2 mm. long, and bears four pairs of short stumpy feet on the thorax. The head bears a proboscis and a pair of short antennæ. It has no pathological significance.

(4) *Ixodes ricinus* (*hominis*), or wood-tick, is also an occasional parasite of the skin. It buries its proboscis in the tissues and sucks its fill of blood. It belongs to the *Acarina*, as do also the American *I. unipunctata* and *I. bovis*.

(5) *Pentastoma denticulatum* (Fig. 88). This is an arachnoid, which in its larval state lodges in the internal organs. Its body is 4–5 mm. long, 1.5 mm. broad, squat and rounded, and possessing some ninety annular segments which are beset with spines at their margins.

The mouth is surrounded by four large hooks in chitinous sheaths. The larva chiefly inhabits the liver, more rarely the spleen, intestine, lung, or kidney. When looked for *post-mortem* the animal has generally been dead for some time; it then appears as a nodule as big as a pea, made up of a mortar-like chalky mass with a fibrous capsule. The mass often contains booklets, but seldom the whole animal.

According to Leuckart, *Pentastoma denticulatum* is the larva of *Pentastoma tænioides*, a lanceolate arachnoid inhabiting the frontal sinuses of various animals, chiefly the dog. The female is 60–85 mm. long, the male 16–18 mm.; the breadth of each is about 3 mm. The mature animal resembles the larva, but it has no hooklets.

FIG. 88.—Head-end of Pentastoma Denticulatum. × 40. (From Perls.)

[*Pentastoma constrictum* has also been met with as a larva in the liver and in the lungs (von Siebold; Aitken, "Science and Pract. of Medicine," 1882).]

226. **Insecta.** The parasites belonging to this class are nearly all epizoa. Some settle on the skin for a brief time only, in order to extract nutriment from it; others are stationary and make use of the epidermal structures for the deposit of their eggs. Of the many insects which afflict man we need name only the following:

(1) *Pediculus capitis*, or head-louse. This inhabits the hairy scalp, and extracts from it, by means of its proboscis, the blood on which it feeds. It fastens its eggs to the hairs by means of a chitinous covering. The "nits" are easily seen as small grayish oval bodies, tightly affixed to the hair. The young louse emerges in about eight days, or less. The irritation induces scratching, which may set up somewhat severe inflammation or eczema.

(2) *Pediculus pubis*, or crab-louse, inhabits the hairy parts of the body and extremities, more especially about the genitals. Its mode of life is much like that of the head-louse, but it is smaller, and often more difficult to detect.

(3) *Pediculus vestimentorum*, or body louse, infests the underclothing and lays its eggs there. It passes to the surface of the body merely in order to feed. It is somewhat larger than *P. capitis*.

(4) *Cimex lectuarius*, or bed-bug, infests bedding, bedsteads, old floors and walls, cupboards, etc., and betakes itself to its human victim at night in order to suck blood from him. It produces wheals on the skin.

(5) *Pulex irritans*, or common flea, also draws blood from the skin. At the point attacked is found a small punctiform hemorrhage surrounded

by a reddened areola. More marked swellings or wheals are sometimes formed. The eggs are laid in the crevices and cracks of flooring-boards, in saw-dust, etc.

(6) *Pulex penetrans*, or sand-flea (chigoe or chigger), is found in the sands of South Africa. The female buries itself and lays its eggs beneath the skin, and so produces intense inflammation.

(7) *Culicida* and *Tipulida* (midges and mosquitoes), *Tabanida* (gad-flies), and *Stomoxys calcitrans* also take blood from the skin and excite transient exudative inflammations. Some flies (*Oestrida*) lay their eggs occasionally in accessible body-cavities or in wounds. This occurs oftener among the lower animals than among men. *Oestrus hominis* (a doubtful species) lays its eggs beneath the human skin, and the larvæ (maggots or bots) set up violent inflammation. *Hæmatopota pluvialis* is the Scotch "clegg ;" it attacks men and beasts indifferently.

[The above account has been chiefly taken from Leuckart, "Die menschlichen Parasiten," Leipzig, 1863–76, and second edition, vol. i., 1879–81 ; Heller, "Ziemssen's Cyclopædia," vols. iii., vii.; Klebs, "H. d. path. Anat.;" Perls, "Lehrb. d. allg. Path.," ii., Stuttgart, 1879. Other comprehensive works are—Küchenmeister and Zürn, "Die Parasiten d. Menschen," Leipzig, 1882 ; Davaine, "Traité des Entozoaires," Paris, 1877 ; Müller, "Statistik d. menschlichen Parasiten," Erlangen, 1874 ; Stein, "Die parasitären Krankheiten d. Menschen," vol. i., Lahr, 1882 ; Perroncito, "Parasiti d. uomo e d. animali utili," Milan, 1882 ; Cobbold, "Parasites," London, 1879.]

Scolecida, or Worms.

227. **Nematoda.** The parasitic round-worms and thread-worms are all nematoids. They have slender cylindrical elongated (sometimes filiform) bodies, without segments or appendages. The cuticle is thick and elastic. The mouth is placed at the anterior extremity, and is provided with soft or horny lips according to the species. The intestine is straight and, with the pharyngeal and gastric portions, extends from end to end of the body-cavity, terminating on the ventral surface just in front of the acuminate tail. The genital organs and their orifices are on the ventral side. The female genital orifice is usually placed at about the middle-point of the length ; more rarely it is anterior or posterior to this. The male orifice coincides with that of the anus ; it is provided with a chitinous investment, which serves also as a prehensile organ during copulation. The males are usually smaller than the females Development is direct, and the metamorphic variations slight. The nematoids parasitic on man are some of them harmless inhabitants of the intestine, while others are highly dangerous when they invade the deeper organs.

228. *Ascaris lumbricoides*, the common round-worm or maw-

worm (Fig. 89), is a cylindrical worm with pointed ends; it is light brown or red in color. The female (*A*) is 25–40 ctm. long; the male (*B*) is considerably smaller, and its tail-end is bent into a hook provided with two *spicula* (*c*) or chitinous spines. The mouth is surrounded by three muscular lips bearing very delicate teeth. The female genital orifice (*a*) is anterior to the middle of the length. The eggs, which the female bears in enormous numbers, have when mature a double shell (Fig. 90) surrounded by an albuminous coating. It is about 50–60 micromm. in diameter. The worm is found in all parts of the alimentary canal, but chiefly in the small intestine. When the females are mature great numbers of eggs are shed and are found in the fæces. They are very tenacious of life, and are not killed by drying or freezing. The life-history of the worm is not fully known. It is possible that the eggs, after ejection from the intestine, require to pass through the body of an intermediate host before they can take up their abode in another human body. Their presence in the intestine does not usually give rise to any serious trouble. Only when they are very numerous do they cause intestinal catarrh, vomiting, and nervous irritation, chiefly in children. At times they pass through normal or morbid openings in the intestinal wall, and give rise to more serious disturbances. Thus an ascaris in the common bile-duct may obstruct the outflow of bile and so induce jaundice. Or if it pass through an ulcerated opening into a hernial sac, or into the peritoneal cavity, it may excite inflammation in the corresponding tis-

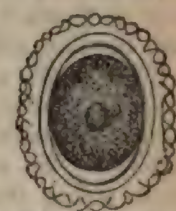

FIG. 90.—Egg of Ascaris Lumbricoides with its shell and albuminous coating.

FIG. 89.—*Ascaris Lumbricoides.* Natural size. (From Perls.) *A*, female; *B*, male, *a*, female genital orifice; *b*, head-end with the three lips, magnified; *c*, male orifice with spicula.

sues. According to Leuckart it may even penetrate the wall of the intestine where there is no pre-existing wound. It is often voided *per anum*, and occasionally *per os* during vomiting.

[*Ascaris mystax*, or round-worm of the cat, is a very rare inhabitant of the human intestine. It is considerably smaller than the common round-worm (Cobbold, " Entozoa," 1864–69).]

229. *Oxyuris vermicularis*, the thread-worm, seat-worm, or maggot-worm (Fig. 91), is a small round-worm. The female (*A*) is 10 mm. long, and acuminate at the tail; the male (*B*) is 4 mm. long and blunt at the tail, which is furnished with a single spiculum at the anus.

FIG. 91. — Oxyuris Vermicularis. (From Leuckart). *A*, female, and *B*, male, magnified fivefold, *C*, egg, magnified 350-fold.

The eggs (*C*), often seen in great multitudes within the body of the female, are 50 micromm. long and 24 micromm. broad. One side is flat and the other rounded. The shell is covered with a thin albuminous coating. The thread-worm inhabits the upper part of the colon and lower part of the ileum. According to Zenker and Heller the mature egg-bearing females affect the colon and cæcum, the younger ones and the males affect the ileum. They are of very common occurrence and are often found in vast numbers. They are apt to migrate from the rectum into neighboring parts, and may so enter the vagina. The irritation they cause induces violent scratching, and this again brings about inflammation of the skin and other disagreeable consequences.

When the eggs have been ejected from the body with the fæces, they must be taken up into the stomach of an animal before they can develop. It is not improbable that the individual host may reinfect himself; for eggs may stick under his finger-nails after he has been scratching himself and may thus be inadvertently carried to the mouth.

The eggs are not destroyed by being dried, and in this condition they may be carried from place to place.

230. *Trichocephalus dispar*, or whip-worm (Fig. 92), is a common but innocuous parasite inhabiting the cæcum and neighboring parts of the intestine. Davaine says that half the inhabitants of Paris are infested with it. Both male and female are 4–5 cm. long. The anterior part of the body is very fine and thread-like. The posterior part, which contains the genital organs, is much thicker; in the female (*B*) it is straight and cylindrical, in the male (*A*) it is rolled into a flat spiral and furnished with a spiculum.

The eggs (Fig. 93) are prolate spheroids, 50 micromm. in length.

They have a thick brown shell, with a peg-shaped glassy-looking projection at each pole.

The first stage of development is passed in water or moist earth. It is very protracted, lasting even in the warm season for four or five months; and in cold weather for a longer time still. The eggs resist cold and drying extremely well.

FIG. 92 A.

FIG. 92 B.

FIG. 93.

FIG. 94.

FIG. 92.—Trichocephalus Dispar. *A*, male; *B*, female. Somewhat magnified. (From Leuckart.) The male is anchored in the mucous membrane by means of his whip-like anterior part.
FIG. 93.—Egg of Trichocephalus Dispar. × 350. (From Heller.)
FIG. 94.—Head-end of Dochmius Duodenalis. Magnified. (From Leuckart.)

231. *Anchylostoma* or *Sclerostoma duodenale* (*Dochmius* or *Strongylus duodenalis*) is a small worm infesting the upper part of the small intestine. The female is cylindrical and 6–18 mm. long, the male 6–10 mm.

The head-end (Fig. 94) is bent toward the dorsal surface and is furnished with a bulging oral capsule. This is cleft almost throughout on the dorsal surface, the cleft being covered by two chitinous lamellæ. On the ventral lip are four curved teeth, on the dorsal lip are two straight ones. These are all held together by chitinous clasp-like structures. Beneath the dorsal cleft a conical projection rises from the interior of the capsule.

The male at its posterior end has a three-lobed bursa, and two thin spicula looking like slender fish-bones. The posterior part of the female becomes gradually thinner and ends in an awl-shaped spine. The vulva lies behind the middle point. The oval eggs are 44–67 micromm. long and 23–40 broad. They pass through their first developmental stages in the human intestine; in the next stages they inhabit dirty or muddy waters; thence they again obtain access to the alimentary tract, and there grow to maturity. Their presence in the small intestine is not free from danger. The worm gnaws into the mucous membrane with its

teeth until it reaches the submucous coat, and thence it sucks its fill of blood. The point attacked is recognizable as a small ecchymosis, in the middle of which is a white spot with a central punctate aperture. This aperture has contained the head. Occasionally small blood-filled cavities are found in the mucous membrane, each containing a coiled-up worm. When present in number these parasites give rise to serious hemorrhages, which produce intense anæmia in the patient (the Egyptian chlorosis). The parasite is common in the tropics. According to Griesinger and Bilharz a great proportion (something like twenty-five per cent.) of the natives of Egypt suffer from it. Wucherer says it is also common in Brazil. McConnell has met with it in India (*Lancet*, 1, 1882). Within the last few years it has been very frequently observed among the workmen engaged in the St. Gothard tunnel.

FIG. 96.—Mature Trichinæ. Magnified. (From Leuckart.) *A*, female; *B*, male.

[References to *Anchylostoma:* Griesinger, "Arch. f. phys. Heilk.," 1854; Wucherer, "Arch. f. klin. Med.," xii., 1872; Bilharz, "Zeitsch. f. wiss. Zool.," iv.; Leuckart, *op. cit.*; Grassi and Parona, "Annali univ. di med.," 1878; Bozzolo and Pagliani, "Giorn. d. Soc. ital. d' igiene," ii., Milan, 1880; Sonderegger, "Corresp. f. schweiz. Aerzte," 1880; Bugnion, "Anchylostome duodénal et anémie du St.-Gothard:" "Rev. méd. de la Suisse rom.," i., 1881; Perroncito, "Arch. p. l. scien. med.," v., Turin, 1881; Long, "Trans. Int. Med. Congress," i., 1881; Mégnin, "Soc. de Biologie," March, 1882; Cobbold, "Human Parasites," 1882, Art. "Sclerostoma," "Quain's Dict. of Med.," 1882.

Among the rarer nematoid parasites are the following. *Eustrongylus gigas* or palisade-worm; the female attains a length of 1 metre, the male of 35 cm.; the color is blood-red. It has been found a few times in the pelvis of the human kidney; but it is commoner in the seal, marten, wolf, and dog. The immature worms dwell chiefly in fresh-water fishes. *Strongylus longevaginatus* (*bronchialis*), a thread-like worm 26 mm. long. It has once been found in the lung of a boy. *Anguillula* (*Rhabditis*) *stercoralis*, a minute round-worm 1 mm. long, indigenous in Cochin-China. It infests the entire alimentary tract, bile-ducts, and pancreatic duct,

and gives rise to chronic diarrhœa. Perroncito (*loc. cit.* and *Micr. Soc. Journ.*, 1882) found it in the tunnel-workmen at St. Gothard. See Perls, "Allg. Path.," ii.; Davaine, "Traité des Entozoaires," 1877; Liebermann, "Dysenterie chronique de Cochin-chine:" "Gaz. des Hôp.," 1877; Normand, "Arch. de Méd. Navale," 1877.]

232. *Trichina spiralis*, or flesh-worm of pork, appears in two forms, according as it inhabits the intestine or the muscles. The intestinal form (Fig. 95) is the sexually mature worm. It is a minute filiform creature, scarcely visible with the naked eye, and white in color. The female (*A*) is 3 mm. long; the male is considerably smaller.

In both sexes the hinder part of the body is straight; the male (*B*) has on the dorsal side of its tail two mammillary protuberances which are turned toward the ventral aspect and include between them four wart-like nodules. There is no spiculum; in copulation the muscular cloaca is everted and protruded.

FIG. 96.—Trichinæ Encysted in Muscle, showing the capsule and its contents. Magnified. (From Leuckart.)

The alimentary canal begins with a muscular pharynx which widens as it passes into the œsophagus. This latter is surrounded throughout its length with a series of large cellular masses. The stomach passes without notable change of structure into the intestine. In the male this terminates, with the seminal ducts, in the cloaca. The testis consists of a tube which commences cæcally at the tail-end, extends forward to the cellular bodies round the œsophagus, and then bends back to be joined by the seminal ducts. The genital organs of the female (*A*) consist of a simple ovary, uterus, and vagina; the latter opens at a quarter of the whole length from the head-end. The ovary, like the testis, is a tube commencing posteriorly and passing forward to join the tubular uterus.

The eggs develop into embryos in the uterus, and these are born in the free state.

The trichina of muscle (Fig. 96) is a small worm 0.7 to 1.0 mm. in

length ; it inhabits the fleshy muscles. It is usually coiled up into a spiral, and lies in a fibrous capsule or cyst, which sometimes also contains calcareous matter. A finely granular substance surrounds the coils of the worm. One capsule may enclose two to five trichinæ.

233. The following is the life-history of the trichina. When a piece of muscle containing live encysted trichinæ reaches the stomach of a host, human or other, the capsule is dissolved and the trichinæ set free. They come to maturity in the intestine in about two and one-half days ; when they proceed to pair. The birth of embryos begins on the seventh day and continues for some time, it may be for weeks. A single worm may bring forth one thousand to thirteen hundred young. These then migrate from the intestine in search of striated muscle. They do so in various ways. Most of them seem to pass directly through the wall of the intestine, the peritoneal cavity, and the subperitoneal connective tissues. Others gain access to the lymph and blood, and are thus conveyed to remote organs. Once in the muscle they penetrate the primitive bundles, reduce the contents to mere detritus, and in fourteen days or so become mature muscle-trichinæ. At first they are only enclosed by the evacuated sarcolemma. Afterward a cyst is formed, consisting partly of a chitinous secretion of the animal, partly of hyperplastic fibrous tissue.

The intestinal trichinæ live but a short time (five to eight weeks). The muscle-trichinæ, on the other hand, may live for a very long time, perhaps indeed for a time limited only by the death of their host. After a while calcareous salts are generally deposited within the cyst ; this gives the cyst a lustrous white appearance by reflected light, and a dark or turbid appearance by transmitted light. If for any reason the trichina dies, the contents of the capsule become calcified.

Trichinæ are met with in man, in the pig, cat, rat, mouse, hamster, pole-cat, fox, marten, badger, hedgehog, and racoon. By feeding on trichinous flesh, muscle-trichinæ may be acquired by rabbits, guinea-pigs, sheep, dogs, etc. Human beings are infected by eating uncooked pork. Trichinosis in man is attended with very various symptoms. Intestinal catarrh follows upon the introduction of the trichinous flesh into the alimentary tract. The invasion of the muscles is marked by swelling, œdema, partial paralyses, and not uncommonly fever. The symptoms are at their height in the fourth or fifth week. Death not unfrequently ensues. The violence and gravity of the symptoms depend generally on the number of trichinæ which have entered the muscles.

The trichinæ are found most abundantly in the diaphragm, intercostal, cervical, and laryngeal muscles ; they are least abundant in the muscles of the limbs. They are usually crowded together at the points of attachment of the muscle to its tendon.

[The worm was first discovered by Paget, at St. Bartholomew's Hospital, in 1834 ; see *Lancet*, 1, 1866. Owen named and described it shortly afterward.

The literature of trichinosis is very abundant; we can only refer to a few of the chief works on the subject.

Owen, "Zool. Soc. Trans.," 1835; Zenker, "Virch. Arch.," vol. xviii., "Arch. f. klin. Med.," viii.; Virchow, "Die Lehre von den Trichinen," Berlin, 1866; Leuckart, "Die Parasiten des Menschen;" Heller, "Ziemssen's Cyclopædia," vol. iii.; Cobbold, "Entozoa," 1869; Glazier, "Report on Trich.," Washington, 1881; Wendt, "Chronic Affect. following Trich.:" New York *Medical Record*, 1879. For further references see Cobbold, "Human Parasites," 1882.]

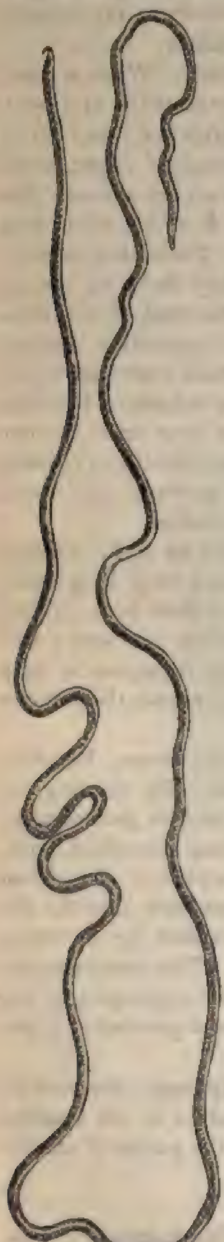

FIG. 97.—Filaria (Dracunculus) Medinensis. Natural size. (From Leuckart.)

234. *Filaria* (*Dracunculus*) *medinensis* (Fig. 97), or Guinea-worm, is a fine thread-like worm from sixty to one hundred cm. in length. Only the female is known. The anterior end is rounded; the posterior terminates in a pointed tail curved over ventrally. The outer covering consists of a firm cuticle thickened at the head-end into a kind of shield. The intestine is narrow, and there is no anus. The gravid uterus occupies nearly the whole of the body-cavity. The embryos have no envelope; they have a stout cuticle and an acuminate tail. They use as intermediate hosts certain small crustaceans (*Cyclops*) that inhabit drinking-water, and so they ultimately reach the human stomach. In Africa and Asia they are very common. They develop to maturity under the skin, giving rise to cutaneous abscesses. They are most commonly found in the legs and feet, especially in the neighborhood of the heel.

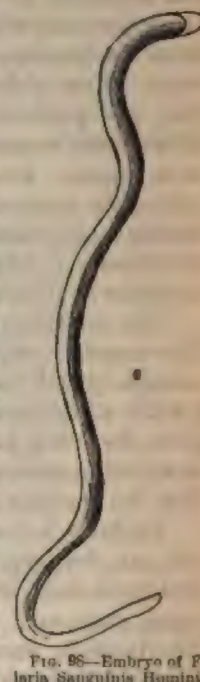

FIG. 98—Embryo of Filaria Sanguinis Hominis × 400. (From Lewis.)

[See Leuckart, *op. cit.;* Davaine, "Entozoaires," etc.; Cobbold, "Entozoa," 1864. The Guinea-worm disease has been identified with the *dracontiasis* of Plutarch, and with the endemic disorder attributed to "fiery serpents" in the book of Numbers.]

235. *Filaria sanguinis hominis* (Lewis), or *sanguinolenta*, in its sexually mature form is a filiform worm 8 to 10 ctm. long. According to Manson it inhabits the lymphatics, especially those of the scrotum and lower limbs. It gives rise to obstructions of the lymph-current and to peculiar inflammations, which end in elephantiasis of the tissues with œdema and lymphangiectasis. Suppurative inflammations, lymphatic abscesses, buboes, chylous hydrocele, and chylous ascites have all been observed as consequences of its presence.

The embryos, which are about 0.35 mm. long (Fig. 98), pass from the lymphatics into the blood and induce hæmaturia and chyluria. Both conditions result from the lodgement of the embryos in number within the kidneys. The embryos may be ejected with the urine. Manson finds that they are spread by the agency of mosquitoes, who take up the filariæ with the blood they suck. The filariæ pass through an intermediate developmental stage in the body of the mosquito; thence they pass into water, and thence again into the human body. It is thus probable that they reach the vessels and tissues from the intestine.

The *Filaria sanguinis* appears to be indigenous only within the tropics (Brazil, Egypt, India, Guadaloupe, etc.).

[See Lewis, "On a Hæmatozoon Inhabiting Human Blood: its Relation to Chyluria and other Diseases," Calcutta, 1872; *Lancet*, 2, 1877; *Quarterly Journal of Microscopic Science*, 1879; Art. "Chyluria:" "Quain's Dict. of Med.," 1882; Bancroft, "Trans. Path. Soc.," 1878; Manson, *Lancet*, 1, 1878, and "Trans. Path. Soc.," 1881; Cobbold, "Parasites," 1879, and "Human Parasites," 1882; *Journal Quekett Microscopic Club*, 1880; Barth, "Annales de Derm. et Syph.," 1881.

Several other rare species of *Filaria* are known. References to them will be found in the standard works of Leuckart, Davaine, and Cobbold, already cited.]

236. **Trematoda.** The flukes, or suctorial worms, are flattened or tongue-shaped worms. They possess suctorial pores by which they can adhere to surfaces, and in some cases they have also hook-like processes. The intestine is usually bifurcated, and terminates cæcally. The development is direct or by alternate generations. In the latter case an intermediate host is necessary. This is usually a mollusc; while the mature worms almost all find lodgement in vertebrate animals. The intermediate larval stage is usually preceded by a period of active locomotion. The trematode larvæ are furnished with a propelling tail, and swim about freely as *cercaria*.

237. *Distoma hepaticum*, the liver-fluke (Fig. 99), is a leaf-shaped trematode 28 mm. long and 12 mm. broad. The head-end projects like a beak, and bears a small suctorial disc in which the orifice of the mouth is visible. Immediately behind this, on the ventral surface, is another suctorial disc. The genital orifice lies between the two discs.

The uterus is a convoluted tube lying behind the posterior disc. The ovaries lie on each side of the hinder part of the body, and between them lie the deeply bifurcated testes. The intestinal canal is also bifurcated and much branched.

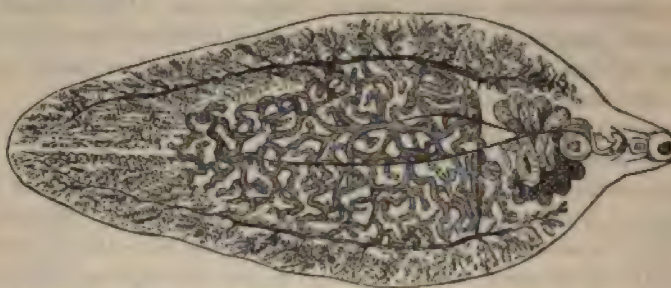

FIG. 99.—Distoma Hepaticum, with Male and Female Genital Organs. × 2½. (From Leuckart.)

The eggs (Fig. 100) are oval, 0.13 mm. long and 0.08 mm. broad. When placed in water a globular embryo is developed, which swims freely by means of its ciliated envelope. The details of its life-history are not certainly known. The adult animal infests the biliary ducts; more rarely it is found in the intestine or in the vena cava. It is rare in man,

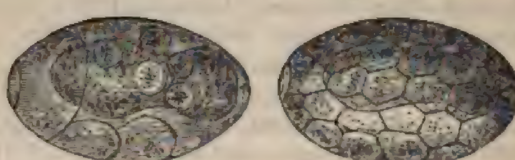

FIG. 100.—Egg of Distoma Hepaticum. × 200. (From Leuckart.)

but very common among the ruminants; it causes the "rot" in sheep. The consequences of its invasion, especially in great numbers, are obstruction of the biliary ducts, accumulation of bile, dilatation and incrustation of the ducts with biliary matters, inflammation around them, and hyperplasia of the hepatic connective tissues, with associated atrophy of the liver-cells.

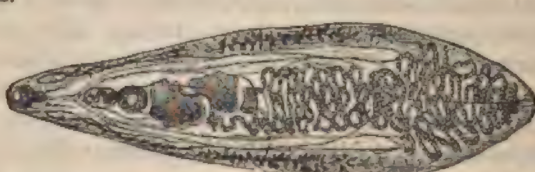

FIG. 101.—Distoma Lanceolatum, with its Internal Organs. × 100. (From Leuckart.)

238. *Distoma lanceolatum* is only 8 or 9 mm. long and 2 to 2.5 mm. broad. It is lancet-shaped, and the head-end does not markedly project. The integument is naked. The two lobulated testes lie close behind the posterior disc and in front of the ovary and uterus; the coils of the lat-

ter are seen through the transparent body-walls. The more anterior coils, which are filled with eggs, look black, the remaining coils are russet-colored. The yellowish-white ovaries lie about the middle of the lateral margin.

The eggs (Fig. 102) are 0.04 mm. long. The embryo is visible in

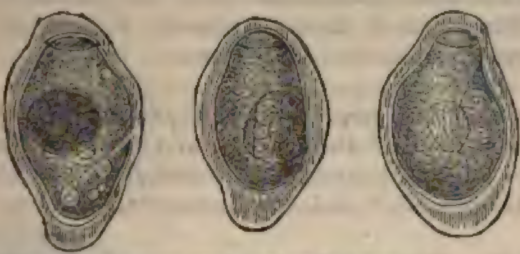

FIG. 102.—Eggs of Distoma Lanceolatum shortly after the Shell is formed. × 400. (From Leuckart.)

them before they have left the uterus, but it only escapes some weeks after they are deposited. Its metamorphoses are unknown. This fluke, like the other, infests the biliary ducts, but it is rarely found in man. It is commonest in sheep and cattle, but as it is usually present in small numbers, it rarely gives rise to any grave disturbances of health.

239. *Distoma hæmatobium*, or *Bilharzia hæmatobia* (Fig. 103), is a species of fluke in which the sexes are distinct. The oral and ventral discs are close to each other, and the fore-end of the body is slender. The sexual orifice in each sex lies just behind the ventral disc. The male is 12–14 mm. long. The body is flattened, but its posterior part is rolled laterally into a kind of tube or gynæcophoric canal (Fig. 103) into which the female is received. The female is 16–19 mm. long and almost cylindrical in form. The eggs are prolate (Fig. 104) and 0.12 mm. long. They are furnished with a spine which may be either terminal or lateral.

FIG. 103.

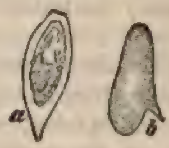

FIG. 104.

FIG. 103.—Distoma Hæmatobium, Male and Female, the latter within the Gynæcophoric Canal of the former. × 10. (From Leuckart.)

FIG. 104.—Eggs of Distoma Hæmatobium. × 150. (From Leuckart.) *a*, with terminal spine; *b*, with lateral spine.

These worms are found in the branches and main stem of the portal vein, in the splenic vein, in the mesenteric veins, and in the vessels of the rectum and bladder. They feed on the blood, and infest man and the monkey. They are very common in Egypt and Abyssinia, the Cape,

and Natal, where they give rise to the disease known as "endemic hæmaturia." The cercaria abound in canals and rivers, and gain access to the body in drinking-water. The embryos mature quickly and permeate the mucous and submucous coats of the ureters, bladder, and rectum, and occasionally the substance of the liver. They set up inflammation of the bladder and ureters, associated with ulcerations, incrustations, and concretions. Hæmaturia is always produced. Cylindrical ciliated embryos may develop within the urinary tract.

[References: Griesinger, "Arch. f. phys. Heilk.," xiii., 1854; Bilharz, "Wien. med. Woch.," 4 and 5, 1856, and *Brit. and For. Med.-Chir. Rev.*, 1856-58; Sonsino, "Arch. gén. de méd.," 1876; Cobbold, "Parasites," 1879; Guillemard, "Endemic Hæmaturia," London, 1882.]

240. **Cestoda.** The cestoids, or tape-worms, are flat compound "worms," destitute of a mouth or alimentary canal. They multiply by gemmation from a pyriform "head" or "nurse." The budded individuals or segments remain for a long time connected with the head, forming a jointed chain. The several members (*proglottides*) of this colony are hermaphrodite. The older segments increase in size as they are gradually pushed away from the place at which they were formed by the constant development of new segments. In other respects they resemble each other exactly; while the head is distinguished by possessing two or four suckers or *oscula*, and generally a circlet of claw-like hooks. By means of these the tape-worm fastens itself to the intestinal wall of its host, which is probably always a vertebrate. The head develops from a rounded embryo having four to six hooklets. These embryos (*proscolices, hydatids*) are found in the various parenchymatous organs of the intermediate host; and thence by what we may call passive migration they reach the intestine of their final host.

The cestoids parasitic on man belong to the families of *Tæniada* and *Bothriocephalida*. The former infest man both as hydatids and as tapeworms; the latter only as tape-worms.

[The development of the Cestoda is exhaustively treated in the handsome work of Hein, "Die parasitären Krankheiten des Menschen," 1882; see also Davaine, "Les Cestoïdes:" "Dict. ency. sciences méd.," 1874; Cobbold, "Tapeworms," 1874.]

241. *Tænia solium* when fully developed is two to three metres long. The head (Fig. 105, *A*) is the size of a small pin-head; it is globular and the suckers project somewhat. The vertex is not uncommonly pigmented, and is surrounded with a pretty large *rostellum* or circlet of some twenty-six hooks (Fig. 105, *B*). The hooks are short, broad, and appressed, with a small projection at the root. The head is followed by a filiform neck an inch or so in length. At a certain dis-

tance from the head the joints begin to be traceable. The first joints are very short, the more advanced ones are longer (Fig. 106); they then become square, and finally the length is greater than the breadth. About 130 ctm. beyond the head the mature segments begin, though the sexual organs have been fully developed in earlier segments. The ripe segments (Fig. 107) are 9–10 mm. long and 6–7 mm. broad; their corners are rounded off. The genital opening lies at the side, somewhat behind the middle. The ovary has seven to ten lateral branches, separated by considerable intervals; each branch breaks up into a series of dendritic ramifications. The ovary is filled with eggs. The parenchyma of the body, both in ripe and unripe segments, is divisible into a peripheral and a central layer. The central layer contains the generative organs and the

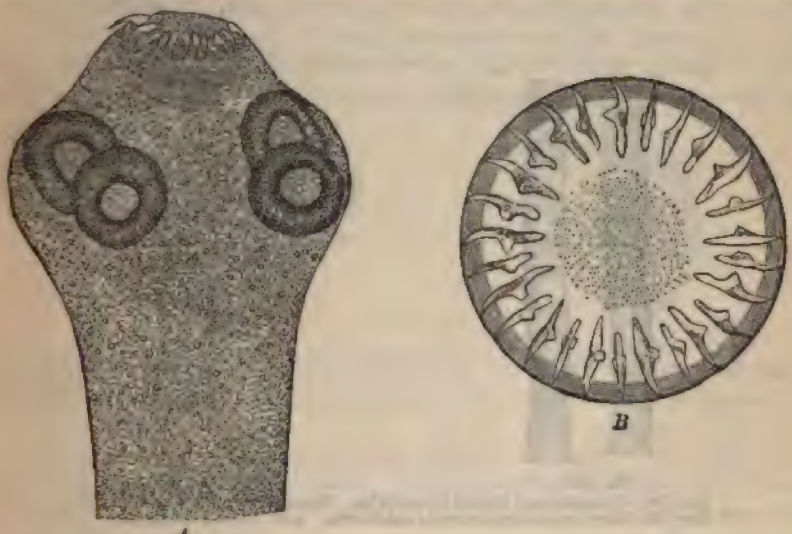

FIG. 105.—*A*, head of *Tænia Solium*, with rostellum protruded. × 50. (Carmine staining; mounted in Canada balsam.) *B*, circlet of hooks magnified. (Leuckart.)

water-vascular system. The latter is an excretory apparatus; it takes the form of two lateral canals running along the margins of the entire chain of segments, and connected by cross-canals at both ends of each segment. Fine ramifications pass from these into the parenchyma.

The male and female sexual organs lie close to each other. The testis is a clear or whitish convoluted tube with vesicles, lying in the forepart of the segment. It passes into the vas deferens, and this into a *cirrus* or retractile extremity, which is rolled up within a muscular pouch or cloaca at the middle of the lateral margin. The cirrus can be everted and protruded through the genital orifice. The opening of the female organ lies close behind the male opening in the same genital cloaca. From this the vagina passes backward toward the hinder border of the segment. Before reaching the border it communicates with a copulative

sac or *receptaculum seminis*, and receives the duct of the germ-bearing organ or true ovary. Then turning forward it passes into an oviduct, into which opens the duct of the so-called vitelligenous organs. The entire ovigenous organ (which must be studied in unripe segments) is thus made up of an unpaired germ-bearing portion or true ovary, and a pair of yolk-bearing or vitelligenous glands, all lying in the hinder part of the segment. The oviduct having received the ducts of these glands passes then into the dilated matrix or uterus, which in sexually mature segments forms a simple straight tube. The egg-germs, leaving the true ovary, become impregnated by spermatozoa from the seminal receptacle, and passing onward are invested with yolk-substance from the vitelligenous glands. Being then complete ova they pass into the uterus,

FIG. 106.

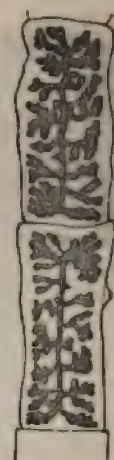

FIG. 107.

FIG. 106.—Immature and Mature Proglottides. Natural size. (From Leuckart.)
FIG. 107.—Two Proglottides, showing the Uterus. × 2. (From Leuckart.)

which as it gradually fills throws out the numerous lateral cæca characteristic of the ripe segment. As this happens the other generative organs gradually disappear.

The peripheral layer is essentially muscular, but it contains a greater or less number of calcareous granules. These, indeed, are not entirely absent in the central layer. The muscular tissue is made up of non-striated fibres ; in the neighborhood of the sucking-discs of the head they form peculiar bunches or groups. The surface of the tape-worm is covered with a transparent cuticle, from which the hooklets of the head are developed.

242. The egg-germs, as they leave the ovary, are pale, thin-walled, spherical cells. In the oviduct they are transformed into yellowish globules, which become covered over with a somewhat opaque envelope or shell thickly beset with minute spicula (Fig. 108, *a*). It is frequently found to be invested by a second covering (*b*), made up of an albuminous

layer with granules, and enclosed in a fine membrane (primitive vitelline membrane). Without this envelope the egg is 0.03 mm. in diameter. With the second envelope the egg already contains the partly developed embryo, whose six hooklets can be distinguished. Thus the embryonic development begins within the uterus; the ripe segments are in fact viviparous animals.

The further development of these embryos, which are now enclosed in a brownish envelope, does not take place within the body of the original host; they must pass into a new one. When they reach the stomach of a pig, the envelope is dissolved, and the liberated embryo bores its way into the wall of stomach or intestine. Thence it migrates, either by way of the vessels or directly, into one or other of the organs. When at last it settles, it passes through various metamorphoses, and at the end of two or three months is transformed into a vesicle filled with serum (Fig. 109), from the inner surface of the wall of which springs a new head or scolex, enveloped in a second membrane or *receptaculum scolicis*.

a b

FIG. 108.

FIG. 109.

FIG. 108.—Eggs of Tænia Solium. × 300. (From Leuckart.) *a*, without the primitive vitelline membrane; *b*, with it.

FIG. 109.—Cysticercus Cellulosæ, with the head and its membrane. Natural size. (From Leuckart.)

This cyst or vesicle containing the head of the tape-worm is called a "measle" or *cysticercus cellulosæ*. The scolices have already their circlet of hooks, sucking-discs, water-vascular system, and calcareous granules. If the scolex reaches the stomach of a man, the cyst-membrane is dissolved, and from the scolex is developed a chain of proglottides, forming a new tape-worm.

243. *Tænia solium* inhabits the small intestine of man, and is acquired by eating ill-cooked pork. The corresponding measle is found in man and in the pig exclusively, or nearly so. In the intestine the worm is generally solitary, but cases in which two or more have co-existed are not very rare. In some instances from thirty to forty have been found in one person. The tape-worm gives rise to irritation of the mucous membrane, colic, and reflex nervous disturbances.

The measle or cysticercus also occurs in man, as we have already indicated. It is found in the most various tissues, in the muscles, brain, eye, skin, etc. Its pathological significance depends on its seat; but it is usually slight. Even in the brain it does not always give rise to serious consequences. It excites a local inflammation which induces a fibrous thickening of the tissues round the cyst. It maintains its vitality for

years. After the death of the scolex the cyst shrinks, and chalky masses are deposited within its cavity. The booklets may be found long afterward. Cystic infection depends necessarily on the introduction of eggs or proglottides into the stomach.

FIG. 111.

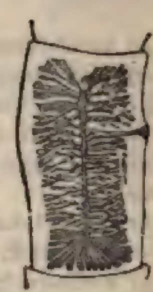

FIG. 110.

FIG. 112.

FIG. 110.—Fragments of a *Tænia Saginata*. Natural size. (From Leuckart.)

FIG. 111.—Head of *Tænia Saginata* Retracted, with Dark Pigment in and between the Sucking-discs × 30. (Unstained glycerine preparation.)

FIG. 112.—Segment of *Tænia Saginata*. × 1½. (From Leuckart.)

[*Cysticercus racemosus* is a measle of the brain. It is distinguished by the fact that it remains sterile and forms grape-like bunches of vesicles (Heller, "Ziemssen's Cyclopædia," vol. iii.; Zenker, "Henle's Beiträge," Bonn, 1882).

Abnormalities of development are very often observed in individual tape-worms.]

244. *Tænia mediocanellata* or *saginata* exceeds *T. solium* not only in length (it may reach four metres) but in width and thickness, as well as in the size of the separate proglottides (Fig. 110, p. 348).

The head (Fig. 111) has neither hooklets nor rostellum. Its vertex is smooth and furnished with four large sucking-discs, usually surrounded with a dark pigmented border.

The eggs are like those of *T. solium.* The uterus (Fig. 112) has a large number of lateral diverticula, running close to each other and branching dichotomously, not like *T. solium* in dendritic ramifications. The genital opening lies below the middle of the lateral margin. The segments which break loose are generally empty of eggs.

The corresponding cysticerci infest the muscles and organs of cattle. The development follows the same course as in the case of *T. solium.* Malformations of the worm are very frequently observed.

Man acquires this tape-worm by eating uncooked beef. It is more widely diffused than *T. solium.*

[*Tænia cucumerina* or *elliptica* is fifteen to twenty ctm. long; its head has a circlet of hooks and a rostellum. It is often found in cats and dogs, rarely in man. Its cysticercus infests the dog-louse.

Tænia nana is a small tape-worm fifteen mm. in length; its head has four sucking-discs and a circlet of hooks. It has been found in Egypt.

The frequent malformations to which *Tænia* is subject have led to the multiplication of species, or rather of specific names. Many of these refer to what are at best mere varieties.]


FIG. 113.—Full-grown Tænia Echinococcus. × 12. (From Leuckart.)

245. *Tænia echinococcus* inhabits the intestine of the dog. It is 4 mm. long, and possesses only four segments, of which the last is larger than all the rest of the body (Fig. 113).

The hooklets have a blunt process at the base, and are seated on a somewhat prominent rostellum. There are some thirty or forty of them. Only the cystic form or hydatid is known to occur in man; he acquires it by the introduction of the eggs into the alimentary canal.

When the embryo migrates from the intestine to some other organ, it is transformed into a cyst incapable of active motion. The **hydatid cyst** consists of an external lamellar highly elastic cuticle, and an internal lining of body-parenchyma consisting of granular matter, cells, muscle-fibres, and a vascular system. When the cyst reaches the size of a walnut (or in some cases sooner) it begins to develop from the parenchymatous layer a series of smaller vesicles (brood-capsules). The wall of these is likewise twofold; but the cuticular layer is within and the parenchymatous layer without.

On these brood-capsules develop numbers of heads or scolices (Fig. 114). According to Leuckart they are formed out of sacculated outgrowths from the external wall of the capsules (see the left side of Fig. 114).

When the rudimentary head has become fully developed into a scolex (sometimes even sooner), it is retracted within the cyst, which it thereby invaginates (Fig. 114). What was before the internal or cuticular surface of the head now becomes the outer surface. The original outer surfaces, which are parenchymatous, come now into contact and adhere to each other. The head is then about 0.3 mm. long, and has a rostellum with tiny blunt hooklets, four sucking-discs, a water-vascular system, and numerous calcareous granules in its parenchyma. The fore-part of the body is often invaginated within the hind-part.

FIG. 114.—Brood-capsules of Echinococcus in connection with the Parenchymatous Layer of the Cyst. × 50 circa. (From Leuckart.) Some of the capsules are closed, some have been burst open in making the preparation.

In many cases these echinococcus-cysts remain single. The only change they undergo is that they grow larger as fresh capsules and scolices are formed, so that they at length reach the size of a big orange, or of the closed fist. The surrounding tissues form, by condensation and thickening, a pseudo-cyst round the cuticular membrane. The cavity of the cyst is filled with clear liquid, which is not coagulable by heat or acid. The brood-capsules are always seated on the inner surface, unless they are shaken loose mechanically. They appear as small white points lying in the transparent parenchyma. Occasionally the cyst may remain altogether sterile.

246. In many cases "daughter-cysts" are formed. They develop in the thickness of the cuticle independently of the proper parenchymatous layer. Between two lamellæ of the cuticle is formed an aggregation of granules which becomes surrounded with a secondary cuticle. This forms the starting-point of a new series of layers. As the layers multiply the inner cavity increases in size and its contents at length become clear and liquid. As the daughter-cyst grows it forces out the wall of the parent cyst like a hernial sac, until it at length gives way and sets the daughter-cyst free. Escaping thus into the tissues round the parent cyst it receives from them an external fibrous envelope, and proceeds to develop brood-capsules in the same way as the primary cyst derived from the six-hooked embryo.

An echinococcus which is thus reproduced exogenously is called *Echinococcus granulosus* or *scolecipariens* (Küchenmeister). It is also described as *E. veterinorum*, as it often occurs in domestic animals.

A second compound echinococcus is the *E. hydatidosus*. It is characterized by the formation of internal daughter-cysts. Naunyn ("Dorpat. med. Zeitsch.," 1870) asserts, and Leuckart agrees with him, that the scolices and brood-capsules may undergo a cystic transformation, and so become daughter-cysts. Naunyn goes on to say that these endogenous daughter-cysts may migrate from the parent cyst and so produce the *E. granulosus*; but this Leuckart disputes. The internal daughter-cysts sometimes develop daughters of their own or "granddaughter-cysts." Each of the cystic forms of which mention has been made may reach to a very considerable size.

247. The third form, or *Echinococcus multilocularis*, only forms small cysts, from the size of a millet-seed to that of a pea. They are always present in very large numbers.

The *E. multilocularis* appears as a hard tumor, seated in the liver. It is built up of a multitude of alveoli separated by dense scar-like fibrous tissue. The contents are transparent and jelly-like or semi-fluid. The alveoli are spherical or irregular in form. Here and there the tissues may have softened and broken down, and thus ulcerated cavities are formed. In other places the vesicles are shrunken and calcified, or the tissues are bile-stained. The distinct alveolar texture of the growth led to its being regarded as a tumor, and it was described as **alveolar colloid** of the liver. Virchow ("Verh. d. phys. med. Ges. zu Würzburg," vi., 1855) was the first to make out its real nature, and he showed that the colloid masses were made up of echinococcus-cysts. The smallest vesicles merely contain granular matter, the larger contain liquid. The granular pseudo-parenchymatous covering of the cuticle seldom contains scolices, most of the cysts being sterile.

E. multilocularis is possibly an abnormal variety or "sport" from the exogenous form.

[References: Virchow, "Virch. Arch.," vol. vi.; Leuckart, "Parasiten," vol. i; Klebs, "Handb. d. path. Anat.;" Bollinger, "Deutsche Zeitsch. f. Thiermed.," ii., 1875; Proujeansky, "Die multiloculäre Echinococcusgeschwulst," In. Diss., Zurich, 1873; Morin, "Deux cas de tumeurs à échinocoques," In. Diss., Berne, 1875; Huber, "Arch. f. klin. Med.," i., iv., v., xxix.; Waldstein ("Virch. Arch.," vol. lxxxiii., with beautiful illustrations) brings forward evidence to show that the dissemination of the echinococcus may be effected through the lymphatics of the liver. He gives full references to previous memoirs.]

248. The occurrence of hydatids in man implies that the eggs of the corresponding canine tape-worm have somehow gained access to his body. The liver is the commonest seat, but hydatids are found in all organs.

Apart from the local inflammation and fibrous hyperplasia they induce, they often cause no trouble to the patient. When a hydatid reaches a certain size, it sometimes dies and the cyst shrivels up. Its contents are changed to a fatty or cheesy mass, often becoming mortar-like as it calcifies. The hooks remain for a long time unchanged.

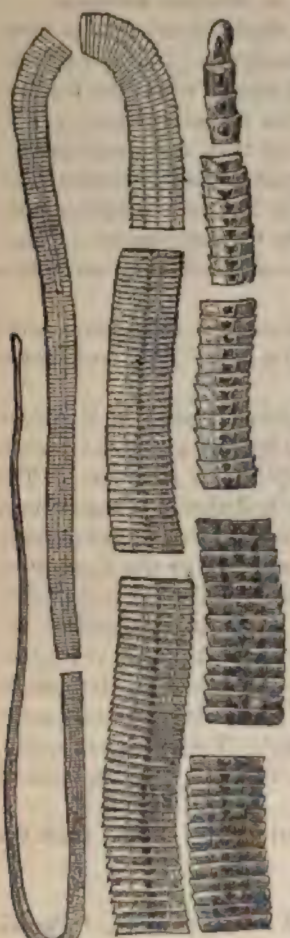

FIG. 115.—Fragments of a Bothriocephalus Latus. Natural size. (From Leuckart.)

In other cases the hydatid becomes larger, especially when it forms exogenous or endogenous daughter-cysts. It may then become dangerous by its mere size. Sometimes if the cyst is wounded or bursts, its contents pass into one or other of the body-cavities and set up severe inflammation. It may even break into a blood-vessel. In the most favorable case it breaks into the intestine or upon the exterior of the body.

The *Echinococci* are widely diffused, but not very frequent; they are commonest in Iceland, where the inhabitants are in constant contact with their dogs. It is somewhat surprising that the multilocular variety is chiefly observed in Switzerland and Southern Germany.

[Neisser gives a summary of the various cases of hydatids that have been published ("Die Echinococcus-krankheit," Berlin, 1877). See also Perls, "Handb. d. allg. Path.," ii.]

249. *Bothriocephalus latus* is the largest of human tape-worms. It measures five to eight metres in length, and consists of three to four thousand short wide segments (Fig. 115). The largest segment is about 3.5 mm. long and 10 to 12 mm. broad. Toward the "tail" the breadth diminishes and the length increases. The body is thin and flattened like a ribbon. The central part of each segment projects somewhat; it is here that the uterus lies, in the form of a simple tube coiled into numerous convolutions. When this is full of eggs the coils lie in contiguous loops, forming a kind of rosette. The genital openings are in the mesial line of the ventral surface, somewhat anteriorly; the female opening being close behind the male.

The testis consists of a series of sacculations lying along the lateral margins of the central layer of the body. The general structure of the body resembles that of the Tæniada.

Anteriorly the worm becomes gradually more and more slender and at length thread-like. The head, which is 2.5 mm. long and 1 mm. broad, is club-shaped or oval in outline, and somewhat flattened. Along each lateral margin is a chink-like suctorial groove.

The eggs (Fig. 116) are oval; they measure 0.07 mm. by 0.045 mm. They have a thin brown shell furnished at the anterior pole with a lid or cap, which is in general easily seen.

FIG. 116.—Eggs of Bothriocephalus Latus. (Leuckart.) One is emptied of its contents and shows the lid.

B. latus occurs chiefly in Switzerland and in the northeast of Europe; it is occasionally met with in Ireland. It lives like the Tæniada, in the small intestine. The first development of the eggs takes place in water. After some months an embryo is hatched, which is provided with six hooklets and a ciliated cuticle. This enters the body of the pike, the trout, or the eel-pout (*Lota vulgaris*) (Braun, "Virch. Arch.," vol. lxxxviii.), and develops in the muscles or viscera into an asexual tape-worm. If it thence reach the alimentary canal of man, it proceeds to develop further and becomes sexually mature.

[It has been maintained that *B. latus* represents the mature form of the cestoid of the trout, known as *Ligula nodosa*. See Duchamp, "Les Ligules," Paris, 1876; Kiessling, "Troschel's Arch.," 1882.

In Greenland another form, *B. cordatus*, occurs. It is only one metre long and has a heart-shaped head.

B. cristatus, two to three metres long, with a crest-like rostellum, has been found in France.]

Protozoa.

250. **Protozoa** are not rarely found in the cavities of the body accessible from without, such as the mouth, lungs, intestine, vagina, etc.; they are most common in patients suffering from chronic disease. The forms observed belong to the *Rhizopoda*, *Infusoria*, and *Psorospermia* or *Sporozoa*, respectively.

Of parasitic *Amœbæ* one species only has been described, the *Amœba coli*. It occurs in the intestine, and is simply a motile cell with a granular protoplasm containing a nucleus and several vacuoles.

[Lösch and Sonsino found the *Amœba coli* in the dejections of a patient suffering from dysentery.]

Among *Infusoria* the *Ciliata* and the *Flagellata* are represented. *Paramæcium* (or *Balantidium*) *coli* is a large ciliated organism occasionally met with in the large intestine and in the fæces. *Cercomonas intestinalis* (Davaine) is a pyriform infusorian, with a spine-like process

at its smaller end and a *flagellum* at its larger end. It is found in the intestine in cases of catarrh, of typhoid, and of cholera. Kannenberg discovered *Cercomonas* in the sputa from a patient affected with gangrene of the lungs. In the same sputa he also found *Monas lens*, a spherical flagellate infusorian. *Trichomonas* is another flagellate infusorian; it is oval in shape and provided with a comb-like row of cilia. One species (*T. vaginalis*) is found in the vagina, another (*T. intestinalis*) in the intestine.

These protozoa are not to be regarded as the exciting cause of the affections with which they are associated. They may possibly, however, maintain or intensify the morbid processes, when present in considerable numbers.

Of parasitic *Psorospermia* we have here to mention the *Coccidia.* According to Leuckart, they are when young simple non-capsulated inhabitants of the epithelial cells. When they reach maturity they become invested with a kind of membranous capsule. In this condition they leave their first lodging, and generally their host at the same time. Their contents are then transformed into "spores" containing granular masses and peculiar rod-like embryonic forms. The spores are round or ovoid. *Coccidium oviforme* (Fig. 117) is a parasite of the intestine and bile-ducts, especially those of the rabbit. In a few cases it has been found in the human subject. It leads in the liver of the rabbit to the formation of whitish nodules, which may be as large as a hazel-nut. The nodules consist of a puriform or cheesy mass, containing multitudes of coccidia. The granular contents of the coccidium are uniformly spread throughout its body, or rolled into a ball in the middle of it. The changes produced in the human liver by the presence of the parasite, in the few cases observed, have been similar to those met with in the rabbit.

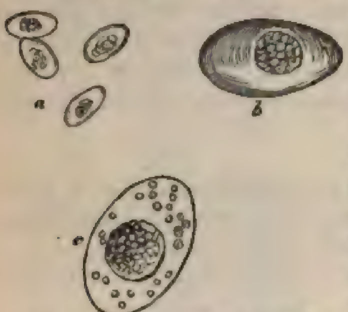

FIG. 117.—Coccidia, from the human liver. *a* is magnified 300-fold; *b* and *c*, 1000-fold. (From Leuckart.)

Our knowledge of the organisms known as "Miescher's cylinders" or "Rainey's corpuscles" is still very defective. They are cylindrical or tube-like bodies, found not infrequently in the muscles of the pig, ox, sheep, and mouse. They contain an innumerable multitude of small oval or reniform corpuscles. Nothing is known of their effect on the human system.

[References to memoirs on *Coccidia* and *Psorospermia* generally: Leuckart, "Die Parasiten des Menschen," second edition; Lieberkühn, "Arch. f. Anat. u. Phys.," 1854; Eimer, "Ueber die ei- oder kugelförmigen Psorospermien der Wirbelthiere," Würzburg, 1870; Klebs, "Virch. Arch.," vol. xxxii.; Stieda, "Ueb. die Psorospermien d. Kaninchenleber:"

"Virch. Arch.," vol. xxxii.; Waldenburg, *ibidem*, vol. xl.; Rivolta, "Dei parasiti vegetali," Turin, 1873.

According to our present information the parasitic protozoa take no important share in the production of human disease. It is, however, not impossible that further research may considerably alter our views in this regard. This is perhaps suggested by the fact that animal parasites are every now and then detected in the blood of vertebrate animals. Thus Rättig ("In. Diss.," Berlin, 1875) describes a ciliated infusorian in frog's blood. Klebs ("Eulenburg's Realencyclop.," Art. "Flagellata") has found in the blood of scurvy-patients very minute organisms, which he refers to the *Infusoria* and names *Cercomonas globulus* and *C. navicula*. Lieberkühn ("Ueb. Bewegung. d. Zellen," Marburg, 1870) found an amœba (*A. rotatoria*) in frog's blood. Lewis (*Quart. Journ. Micros. Science*, xix., 1879) found in rat's blood, and Wittich ("Centralb f. med. Wiss.," iv., 1881) in hamster's blood, a mobile organism resembling the spermatozoon of the frog. Koch ("Mitth. a. d. k. Gesundh.," Berlin, 1881) describes a fusiform granular-looking structure with one or two flagella found in hamster's blood. He regards it as a flagellate infusorian.]

SPECIAL
PATHOLOGICAL ANATOMY.

SECTION I.

BLOOD AND LYMPH.

CHAPTER I.

FUNCTIONS OF BLOOD AND LYMPH.

251. **Blood** and **lymph** are the essential juices of the body. They stand in the closest relation to the vital processes which go on in the tissues. By means of the blood, the constituent elements of the body are supplied with the nutrient substances and the oxygen which they require. By the blood and the lymph are conveyed away the waste and surplus matters which have ceased to be useful to the tissues.

The nutrient substances and the oxygen are derived from without. The former usually enter the body from the alimentary canal, the latter usually through the lungs. But most parts of the body are under certain conditions capable of directly assimilating both nutriment and oxygen. The channels of entrance are in such cases the smaller blood-vessels and lymphatics.

The matters which have to be removed from the tissues are partly surplus nutriment, partly the products of tissue-waste and metabolism. These matters are carried off either to be utilized elsewhere within the system, or to be ejected altogether.

Under normal conditions, the incomings and outgoings balance each other in amount.

The channels by which the normal constituents gain access to the blood and lymph may also serve to admit matters which are noxious or at least abnormal. These matters may be either wholly extraneous, or produced within the body itself in virtue of some morbid or abnormal metabolism. The result of their admission is a more or less enduring pollution of the blood and lymph. In many cases, the blood is able to eliminate them harmlessly and speedily, chiefly by means of the kidneys and the liver; but in other cases, the pollution is more permanent. The composition of the blood often suffers in consequence, and its renovation may not be effected until some of the tissues or organs have been more or less injured by malnutrition.

The abnormal matters which gain access to the blood may be in very various states of aggregation. Most commonly they are in the form of gases or liquids; but the blood is likewise not infrequently polluted by the admission of solid corpuscular matters. These latter have by far the greatest interest to the pathologist, for they are demonstrable by means of the microscrope.

We cannot regard the blood as a liquid whose chemical composition is variable or indefinite. Experiment shows that the proportions of albuminoids, salts, iron, etc., which it contains are constant within narrow limits, and that its composition is maintained by nicely-adjusted assimilation and elimination of material. We must therefore look upon any serious variation from the normal in the composition of the blood as a pathological phenomenon.

The blood is in fact a definite living tissue.

Although the changes that occur in the composition of the blood are by no means so important as were formerly believed, though we no longer consider the juices and "humors" to be the seat of all diseases, yet we should be in error if we regarded the blood as nothing more than a solution of various chemical substances. The blood always contains living cells, and these fulfil definite vital functions. And even if the red corpuscles are so transformed from the ordinary cell-type that some deny their right to the title of living cells, the life and activity of the white blood-cells is unmistakable, and they are an essential constituent of the blood.

In disease, too, the blood comports itself as a living tissue. We may have localized death or necrosis in a solid tissue, and we may likewise have a localized death of the blood. The retrogressive and formative changes in cells and intercellular substance, which we have recognized as the manifestation of diseased function in the solid tissues, have their analogues in the elements of the blood. Many of the morbid processes affecting the blood are thus manifested not merely by changes in its chemical composition, but by simultaneous changes in the form and quantity of its morphological elements; and in many diseases the morbid activity of the white blood-cells plays a highly important part.

CHAPTER II.

INTRAVASCULAR COAGULATION OR THROMBOSIS.

252. We have already seen (Art. 35) that when blood dies it usually coagulates, that is to say—solid masses of fibrin are formed in the plasma, the masses consisting of granules or granular fibrils or homogeneous flakes. When coagulation occurs within the vessels during life the process is called **thrombosis,** and the coagulum is called a **thrombus.**

On SCHMIDT'S hypothesis the coagulation of the blood depends on the union of two albuminoid bodies, fibrinogen and fibrinoplastin (or paraglobulin), in presence of a third factor or ferment (Art. 35). Taking the fibrinogen as furnished by the plasma, and the other factors as furnished by the colorless elements of the blood, coagulation is evidence of the death of the latter in whole or in part.

Coagulation may take place in blood which is at rest, or in blood which is in motion; and the appearance of the thrombus is different in the two cases. In blood at rest coagulation takes place throughout the entire mass simultaneously. The thrombus is thus dark-red or brown in color, and consists of granular and fibrous clots of fibrin containing multitudes of red corpuscles and a few white corpuscles. **Red thrombi** of this kind are most commonly formed in occluded or highly engorged vessels. When recent they are soft and full of serum. Afterwards they become firmer, tougher, and drier, the fibrin contracting and squeezing out the serum. They become at the same time paler and grayer; the decolorization proceeds in fact by the same steps as in extravasated blood (Art. 68).

When coagulation begins in blood which is still flowing, the entire mass does not coagulate at once; minute flakes separate out, consisting chiefly (according to ZAHN) of white blood-cells with a varying number of red blood-cells. According to the number and arrangement of these latter the thrombus may be white or gray, or pale reddish, or mottled and stratified.

In the case of pure **white thrombi,** only the colorless elements of the blood separate out. When the necessary local conditions for coagulation are set up at any spot (on the intima of the heart or of a vessel) the clots adhere to the surface, and gradually increase in size by successive additions. At first the cellular elements of the mass are distinguishable; but in twenty-four hours the outlines of the cells disappear,

and the mass is transformed into homogeneous or finely-granular fibrin.

The thrombus grows by the addition of colorless elements like those in which it began. If red corpuscles are entangled with the others, it may gradually become more and more tinged with red. If the red corpuscles are precipitated *per saltum* or intermittently, the thrombus will exhibit strata of red and white. This alternate precipitation, which leads to the formation of **mottled thrombi**, is most likely to happen if the blood is alternately at rest and in motion at the site of the deposit.

The fundamental investigations on the subject of thrombosis are those of VIRCHOW (*Gesamm. Abhandl.* 1856, *Hand d. spec. Path.* I.), who made out by experiment the conditions of intravascular coagulation and its effects on the circulation. ZAHN has shown (*Virch. Arch.* vol. 62, and *Rev. méd. de la Suisse rom.* 1881) that the formation of a thrombus in the blood-vessel of a frog may be directly observed under the microscope; one has only to injure the vessel mechanically or place on it a crystal of common salt; and coagulation at once begins. In this way the behavior of the white corpuscles has chiefly been made out. Quite recently BIZZOZERO (*Centralb. f. d. med. Wiss.* 1882, *Arch. ital. de biologie* I., and *Virch. Arch.* vol. 90) has observed in living blood certain small colorless disc-like bodies, about half the size of the ordinary white corpuscles. These he calls "*Blutplättchen*" or blood-plates, and regards as identical with HAYEM'S hæmatoblasts (Art. 85). In blood taken from the vessels in the usual way they break up into the knots of granules described by MAX SCHULTZE and others. According to BIZZOZERO coagulation takes place when the blood-plates begin to break up in a liquid containing fibrinogen; and he maintains that they form the essential constituent of white and mottled thrombi. RAUSCHENBACH, a pupil of SCHMIDT'S, has criticised these statements in a recent inaugural dissertation (Dorpat 1882). See also WOOLDRIDGE, *Du Bois-Reymond's Arch.* 1883.

253. **Thrombosis** depends upon two factors; one is the morbid alteration of the vessel-wall, the other the retardation or stoppage of the blood-current. In most cases the two factors are in action simultaneously.

In normal conditions coagulation is prevented by the ever-renewed contact of the blood with the living endothelium of the vessel-wall (BRÜCKE). If the endothelium die in consequence of disease of the inner coat of the vessel, or if the blood is in part prevented from fresh contact with the endothelium by stagnation or cessation of the current, the influences which inhibit coagulation are interfered with. In accordance with this view we find that thrombosis is commonest where there is degeneration or inflammation of the lining membrane of the vessels or the heart, or where the circulation is impeded by such causes as compression or occlusion or dilatation of the vessels, fatty change in the heart, etc. Direct injury of the vessel-wall, if it extend to the intima, likewise leads to thrombosis. If a vessel be perforated by a small opening, the wound is quickly closed by white corpuscles which deposit themselves around and over the opening, while a white thrombus gradually forms and projects into the lumen of the vessel.

The various forms of thrombus are distinguished according to their relation to the lumen of the vessel. **Parietal thrombi** are seated on the walls, **valvular** thrombi on the valves of the heart or of the veins. If the thrombus occludes the vessel it is called **obliterating.** The first deposit is spoken of as primary or autochthonous, the accretions superimposed on it as secondary or induced. By such accretions a parietal thrombus may grow into an obliterating one. In this way, too, it not seldom happens that a thrombus originally white or mottled is covered over with a red thrombus: the first deposit takes place in blood which is still moving, this by degrees occludes the vessel, the current is stayed, and the blood then coagulates as a whole. The reverse occurs when an obliterating red thrombus contracts, and leaves the channel partly free again. Both cases are illustrated in the **marasmic thrombosis** of cachectic anæmic patients; in them the vascular system seems too capacious for the diminished quantity of blood in circulation, and in consequence the current is here and there abnormally slow or ceases altogether.

Thrombosis may occur in any part of the vascular system. Cardiac thrombosis usually begins in the auricles, or in the crevices between the trabeculæ carneæ. In both sites the thrombi start from the deeper folds and involutions of the endocardium, but by continued apposition of fibrin they may grow into large polypoid masses projecting into the cavity, and are then spoken of as **cardiac polypi**. Coagula form in like manner upon the surfaces of inflamed valves. Both the parietal and the valvular forms of cardiac thrombi may grow to a very large size, and fill out the greater part of the auriculo-ventricular cavity.

Thrombosis of the larger arteries may occur in the most various situations. In marasmic patients with highly degenerate arteries parietal thrombi, both white and mottled, may be formed in the aorta and adhere firmly to the inner coat. In the veins thrombi are most commonly formed in the pockets of the valves; whence they grow out and become obliterating thrombi. Or a thrombus primarily formed in a small tributary vein may grow out into the lumen of a larger vein. For example, thrombosis originating in a small vein of the lower limb may ultimately extend continuously till it reaches the vena cava inferior or even the heart itself. Thrombosis of the smallest vessels is usually the result of some disorder of the tissues, chiefly of the nature of inflammation or necrosis.

Post-mortem clots. Thrombi which have been formed during life are in general easily distinguished from clots formed *in articulo mortis* or *post-mortem*. After death the blood usually coagulates in such a way that the red corpuscles are entangled and included in the clots; on post-mortem examination we find the vessels containing soft dark-red gory masses. Sometimes however the corpuscles have time to separate from the plasma before the fibrin is formed; in such cases the clots are soft, moist, somewhat elastic, yellowish, and faintly opalescent. From these somewhat bacon-like clots the true white or mottled thrombi are distinguished by their grayish and more opaque appearance, and by their more or less marked stratification. They are moreover firmer, drier, and less elastic;

when torn across the surface is corrugated or step-like; and finally they adhere to the wall of the vessel and generally distend it (HUMPHREY), while the post-mortem clots are free. Under the microscope the thrombi are seen to contain a larger proportion of white blood-cells than the post-mortem clots.

It is less easy to distinguish red thrombi from red post-mortem clots. The chief characters of the former are their greater firmness and dryness, and their adhesion to the vessel-wall. In less recent thrombi signs of decolorization appear, by which the dark-red of freshly coagulated blood passes into a lighter and brownish-red. Not uncommonly we may find true thrombi overlaid and concealed by post-mortem coagulations.

With regard to the effects of thrombosis upon the circulation see Arts. 22–25 and 30.

254. **Issues of thrombosis.** The fully-developed thrombus is a somewhat firm and dry mass adhering to the lining membrane of a vessel or of the heart, its color and structure varying as we have described. The comparatively small quantity of liquid it encloses is explained by the fact that the fibrin after its separation always shrinks, and so squeezes out the liquid from its meshes. This shrinking, when it occurs in an obliterating thrombus, may leave the channel of the vessel open once more. In many instances the contraction due to shrinking is very considerable. The fibrin is transformed into a dense mass, which may persist unchanged for a long time and ultimately becomes calcified. It is thus that the chalky concretions called **phleboliths** are formed in the veins. In the same way thrombi which are seated on roughened surfaces in the aorta or valves of the heart may become calcified; and may become sheltered from secondary deposits by the growth of an endothelial covering over them.

Contraction with calcification is what we may call a favorable issue of thrombosis. The very common issue of thrombosis in softening is much less favorable. Softening is distinguished as simple or red softening, and puriform or yellow softening. In **simple or red softening** the central parts of the thrombus are first of all changed into a grayish or reddish pulp, consisting of broken-down and shrunken red corpuscles, pigment granules, and colorless granular detritus. If the softening then extends to the surface layers, and if the blood-current is still flowing over the thrombus, the products of disintegration may be carried into the general circulation. This occurs both in the case of cardiac polypi and in venous thrombosis, especially when the tip of a thrombus projects from the orifice of a small vein into the channel of a larger in which the blood is still flowing. The result is the formation of emboli (Arts. 30 and 37, and 257).

The most unfavorable issue of all is the **puriform or yellow softening** of the thrombus. In this case the thrombus is transformed into a dirty or reddish yellow, fœtid, pus-like cream or pulp. This contains a multitude of pus-corpuscles and a large proportion of a finely-granular matter, which consists in part of fatty and albuminous detritus and

in part of micrococci. The latter frequently form groups or colonies, and are probably to be regarded as the exciting cause of the softening process. Such puriform thrombi act destructively on the surrounding tissues and set up inflammation. The intima of the vessel becomes turbid or opaque; and suppurative inflammation begins in the tunica media and tunica adventitia, extending to the tissue inclosing the vessel. Soon the entire thickness of the vessel-wall is infiltrated, and takes on a dirty-yellowish or grayish appearance. Ultimately the tissues undergo putrid disintegration (Art. 291). If the puriform matters are carried by the blood-current to distant spots, they there produce necrotic and putrefactive changes in the tissues, and set up suppurative inflammation.

The entire process, in which puriform softening of a venous thrombus is associated with suppurative inflammation of the vessel-wall, is described as purulent **thrombophlebitis.** It is due in the first instance to the causes which lead to thrombosis, and in the second, to the access of micrococci to the thrombus. In other cases, the inflammation of the vessel-wall is primary, and the thrombosis a secondary effect. The purulent form is most commonly met with in the neighborhood of septic wounds and ulcers.

255. The most favorable issue of thrombosis is in **organization** of the thrombus. By this is meant the replacement of the fibrin and corpuscles by vascularized fibrous tissue.

The new fibrous tissue is mainly the product of an inflammatory process; it is developed from migrated white blood-cells. Regenerative multiplication of the endothelial cells plays but a subordinate part or none at all. The thrombus itself takes no active share in the process; it is a lifeless mass, a foreign body, and as such sets up inflammation in its neighborhood. The inflammation runs the same course as other constructive or plastic inflammations. The histological changes follow exactly on the lines of those described in the Arts. 108–111; and the behavior of the tissues towards the foreign body (the thrombus) is identical with that described in Arts. 112–116. The process by which a thrombus is organized resembles most closely the plastic inflammation of a serous membrane. A blood-vessel has indeed a certain anatomical analogy to the serous cavities, being mainly distinguished by its particular configuration and by the special structure of its walls.

In the first stages of the organizing process we observe that the vessel-wall is here and there infiltrated with small leucocytes, the infiltration appearing in the outer and middle coats (Fig. 118 *e*), as well as in the inner coat (*f*). Presently migratory cells begin to accumulate, partly within the lumen of the vessel (*g*), partly within the substance of the thrombus, and partly between the latter and the vessel-wall. The first cells which migrate are small and round, and their nuclei are strongly stained by coloring reagents. Presently larger cells appear, with clear

vesicular nuclei (*h*); these have been developed out of the migratory cells. They are of various forms, rounded, elongated, or ramified (*h*). These larger cells are the formative or fibroplastic cells. When they have multiplied sufficiently, so that they become contiguous, they are gradually transformed into fibrous tissue. New blood-vessels are simultaneously developed, and at length the new-formed tissue is vascularized throughout.

This is the general course of the process, but considerable variation may take place in details. Thus, if the thrombus result from ligature, in a young and healthy patient, the accumulation of leucocytes will be

FIG. 118.—SECTION OF A THROMBUS IN PROCESS OF ORGANIZATION.

(*From the femoral artery of an aged man three weeks after ligature : hæmatoxylin staining* : × 350.)

a, tunica media.
b, fenestrated elastic membrane.
c, intima thickened by previous inflammation.
d, coagulated blood.
e, cells infiltrating the media.
f, cells infiltrating the intima.
g, leucocytes, partly within the thrombus, partly between it and the intima.
h, various kinds of formative cells.

much more marked than in such a case as is represented in Fig. 118: in this case the patient was old, and his arteries had already undergone a certain amount of morbid change. The accumulation of leucocytes may become so great as to give the thrombus the appearance of a mass of granulation tissue. The duration of the process also varies greatly. By operating on one of the lower animals, we can be sure of finding the thrombus completely vascularized in twelve days. In the case figured above, the first formative cells are developing three weeks after the ligature.

The leucocytes are derived from the *vasa vasorum* and the vessels in the neighborhood of the occlùded vessel. They enter chiefly from the

zone of ligature, at the points where the inner coat is torn through and where the injury to the vessel-wall is greatest. The new vessels are likewise derived from the *vasa vasorum*, though blood channels are also opened up from the side of the unoccluded lumen of the old vessel. The diagram (Fig. 119) may help to make clearer the appearance of an organized thrombus after ligature, and its relation to the walls of the vessel. It represents in a general way a longitudinal section through the cicatrix resulting from ligature.

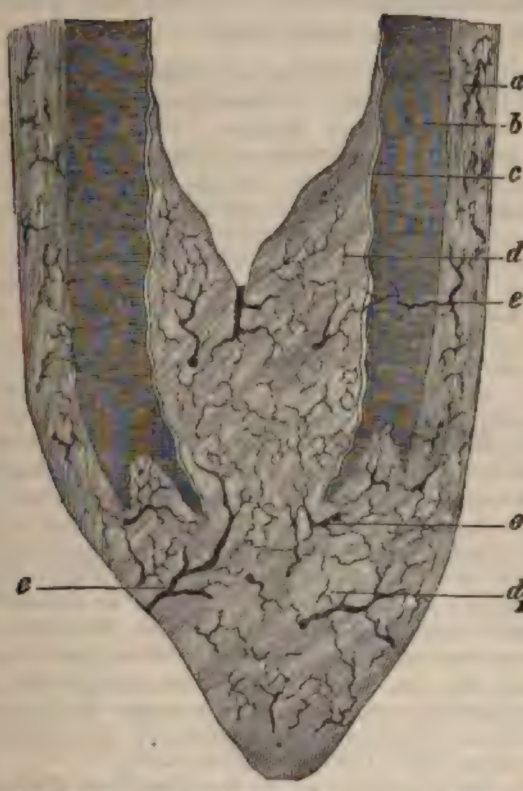

FIG. 119.—DIAGRAMMATIC SECTION OF A LIGATURED VESSEL.

(The thrombus is supposed to be entirely replaced by vascular fibrous tissue.)

a, adventitia.
b, media.
c, intima.
d, new-formed fibrous tissue within the lumen.
d_1, new-formed fibrous tissue outside the lumen.
e, new blood-vessels.

The site of the ligature is seen to be occupied by highly vascular scar-tissue, which is connected with the adventitia outside the vessel (d_1), but is also prolonged into the lumen of the vessel (d), so as effectually to occlude it. Close to the site of the ligature the various coats of the artery blend with the cicatrix. The vessels (e) of the fibrous plug are

chiefly derived from without, but there are also openings in connection with the lumen of the ligatured vessel itself.

As we have said, the endothelial cells take little share in the formation of the cicatrix. At the site of the thrombus itself the endothelial cells have disappeared; there can, therefore, be no question of their multiplication. They can only multiply, if at all, along the line where the thrombus bounds the free lumen of the vessel. From this line they may proceed to cover over the upper surface of the thrombus with an endothelial layer; and it is possible that they may there take some part in the development of the new fibrous tissue.

The organization of thrombi has long been a subject of minute investigation both anatomical and experimental. Of the more recent researches, the following may be named: SCHULTZ, *Deutsch. Zeitschr. f. Chir.* IX., and *Ueb. d. Vernarbung d. Arter.* In Diss. Berne 1877; RAAB, *Arch. f. klin. Chir.* XXIII. (with full references), and *Virch. Arch.* vol. 75; RIEDEL, *Deutsch. Zeitschr. f. Chir.* VI. (1875); BAUMGARTEN, *Die sogen. Organisation d. Thrombus* Leipzig 1877; DURANTE, *Wiener med. Jahrb.* III., IV.; SENFTLEBEN, *Virch. Arch.* vol. 77; TILLMANNS, *Virch. Arch.*, vol. 78; AUERBACH, *Ueber d. Obliteration d. Arterien nach Ligatur*, In. Diss. Bonn 1877; FOÀ, *Arch. p. l. sci. med.* III.; HAMILTON, *Edin. med. Journ.*, 1880–81.

The question most hotly discussed has been whether the white blood-cells are or are not the generators of the new fibrous tissue, and to this various answers have been given. ZIEGLER, from his own investigations, is constrained to side with those who assign the chief share in the formative process to the extravasated leucocytes. The process has been too often regarded as something *sui generis*; the only characters which distinguish it from other pathological tissue formations are that the process takes place within a tube, and that dead tissue is being absorbed as new is being formed. Again the question is asked whether the new tissue is formed by inflammatory granulations or by regenerative or hyperplastic proliferation. The view taken above is that the former is the commoner and the more important mode; but the active participation of the endothelial cells is not excluded. RIEDEL's observation is of interest in this connection; he states that the inner surfaces of an artery may be made to cohere without the formation of a clot, and that, in this case, the vessel is occluded simply by the multiplication of the apposed endothelial cells. This seems to confirm the view we have taken, that it is the presence of the thrombus, together with the mechanical injury to the vessel-wall, which sets up the plastic inflammation.

With regard to the canalization of the thrombus from the lumen of the occluded vessel (a fact insisted on by SCHULTZ), it seems probable that this is not at first a true vascularization; it is rather to be referred to the shrinking of the fibrin, which may give rise to lacunæ in the thrombus. These lacunæ become transformed into blood channels, which by and by become connected with the capillaries originating in the *vasa vasorum*.

256. The account just given applies in the first instance to the organization of thrombi in ligatured arteries. But the process in other cases is exactly similar. If a marasmic venous thrombus of some standing is examined, the inner coating of the vein is found infiltrated with cells, and the margins of the clot are transformed into granulation-like tissue, or even into vascular fibrous tissue. In the case of parietal

thrombi in the larger arteries, or in the aorta, the process of organization is very slow. Even old thrombi may show no distinct sign of organization; and in other instances small patches of immature fibrous tissue may be found on the surface. The thrombi that occupy aneurysmal sacs are very slowly and imperfectly replaced by fibrous tissue.

The process by which **wounds in blood-vessels** are healed up is analogous to organization. SCHULTZ has shown that after hæmorrhage ceases a thrombus composed of cohering white blood-cells occupies the site of the wound. This plug may bulge outwards under the pressure of the blood, but the sinus so formed is again filled up with white blood-cells. These thereupon proceed to develop, new vessels penetrate the mass from the surrounding parts, and a cicatrix is at length produced (Art. 308).

In the course of time, the fibrous tissue which replaces a thrombus shrinks more or less. The plug of scar-tissue formed after ligature may thus become extremely small, the vessel becoming pervious up to the point of ligature. The plug formed in the continuity of a thrombosed vessel may almost disappear, leaving behind only a thickening of the vessel-wall or a few bands or threads across the lumen. When this occurs, the blood may be enabled to flow through the reopened channel without sensible obstruction.

257. In Art. 254, we said that when a thrombus softens and breaks up, fragments of it may be swept off into the blood-current. We said also, that when the softening is puriform, the matters thus swept off excite inflammation and suppuration at the points where they settle. We have next to consider the fate of the less noxious fragments swept off from recent thrombi, especially the looser quickly-growing red kind, or from thrombi undergoing simple softening. Such a fragment, or **embolus,** if it is too large to pass through the capillaries, will become wedged in one or other of the smaller arteries, and generally at a point of bifurcation. Thus, an embolus starting from one of the systemic veins or from the right heart will lodge in a pulmonary arteriole. The first result of the lodgment in the vessel, or **embolism,** is that fresh deposits of fibrin take place on the plug, so that it soon occludes the vessel completely, even if too small to do so originally. The effect on the circulation of occlusion by embolism has already been described (Art. 30).

An embolus may undergo changes analogous to those which take place in the primary thrombus; it may soften, or shrink, or become calcified, or be replaced by fibrous tissue.

The process of organization is the same as that already described, but the volume of the fibrous plug is always very much smaller than that of the original embolus. After some weeks or months, the site of the embolus is often marked by nothing more than a fibrous band or a nodular protuberance on the inner coat of the vessel. In other instances, the

lumen is crossed by numrous threads running singly or connected into a loose network.

But the process is necessarily very different when the embolus sets up destructive inflammation around it. The inflammation then takes the suppurative form; the vessel-wall, the sheath, and the surrounding tissue are successively attacked, and an **embolic abscess** is formed (Art. 291).

CHAPTER III.

CHANGES IN THE QUANTITY AND COMPOSITION OF THE BLOOD.

258. We have already said (Art. 251) that the blood is a liquid tissue whose quantity and composition are normally constant, within narrow limits. This constancy of the blood is maintained by the physiological adjustment of the matter assimilated and the matters eliminated, and by the speedy rejection of any abnormal matters which may gain entrance. In disease, the equilibrium may be disturbed, so that the quantity and the chemical constitution of the blood may deviate from the normal for a longer or shorter time.

Increase in the quantity of blood in the body, *i. e.*, a true hyperplasia or **plethora,** does not occur as an abiding condition. When, for example, after amputation by the bloodless method (in which the blood contained in the limb is pressed back into the body before operation), the quantity in the body is rendered relatively excessive, the surplus is rapidly used up, and is not replaced. True plethora or polyæmia is in fact an essentially transient condition.

The opposite condition, namely, decrease in the quantity of blood, is called **oligæmia** or **anæmia.** Every abnormal loss of blood produces a temporary anæmia. If this does not exceed a certain limit, and if there is nothing to interfere with the production of blood, the loss is soon made up, and the anæmia is transient. But if the loss is greater, or often repeated, or long-continued, the anæmia may become chronic. During life, this condition is indicated by the pallor of the skin and mucous membranes; *post-mortem* it appears in the small proportion of blood contained in the several organs.

After a loss of blood, the replacement of the *liquor sanguinis* proceeds more rapidly than the replacement of the red corpuscles. For a time, therefore, the blood is relatively poor in red corpuscles, a condition described as **oligocythæmia.** This condition is frequently observed in fevers and in cases of lead or mercury poisoning; it is then an indication of impaired nutrition. In other cases, we must assume that the cause lies in the imperfect working of the blood-making organs (Art. 261); but we are frequently unable to say where the fault lies, and then we speak of the condition as **essential or idiopathic anæmia.**

If the elimination of water from the blood be interfered with, as in

renal disorders, the blood becomes watery, and the condition is described as **hydræmia** or hydræmic plethora. Here the watery parts alone are out of proportion; the amounts of the other constituents present are normal.

Hydræmia is less often the result of mere retention of water than of morbid diminution in the proportion of albumen contained in the blood, a condition which has been called **hypalbuminosis.** The diminution depends either on deficient supply or excessive consumption of albumen, or on both together. It is a common result of chronic disorders of digestion, long-continued and profuse discharges from the bowels, dysentery, chronic suppurations, excessive secretion from certain glands (over-lactation), repeated hæmorrhages, loss of albumen from renal disease, discharges from disintegrating tumors, etc. Or, as an idiopathic anæmia, we may be unable to trace its source. The proportion of hæmoglobin in the blood is diminished both in oligocythæmia and in hydræmia. Normally, the blood should contain some 14 grammes of hæmoglobin per 100 cubic centimetres; in anæmia, the proportion may fall to 8, 6, or even 3 grammes. Such blood is limpid, pale, and light-red, having much the look of meat-washings.

In oligocythæmia, the decrease of hæmoglobin is accounted for by the diminution in the number of red corpuscles. When the number is normal, either their size (Art. 261 on microcythæmia) or their hæmoglobin must be reduced. Both cases occur. In the latter case, the individual corpuscles look strikingly pale under the microscope, as is observed in the blood of chlorosis.

Anhydræmia is the opposite of hydræmia; it implies that, while the proportion of albumen in the blood is maintained, the proportion of water and salts is diminished. Blood of this kind appears viscid and tar-like in consistence and color. In man, it is oftenest the result of profuse watery discharges from the bowels, as in cholera, or of excessive loss of water by the skin.

In many diseases, the proportion of the fibrin-factors in the blood is altered. It is increased (**hyperinosis**) in all inflammatory disorders, but especially in croupous pneumonia, rheumatism, and erysipelas. It is commonly somewhat increased in hydræmia. The result is that when the blood coagulates the amount of fibrin formed is abnormally great.

The proportion of hæmoglobin in the blood is subject to considerable variation according to age (LEICHTENSTERN, *Untersuchungen üb. d. Hämoglobingehalt d. Blutes* Leipzig 1878; HOPPE-SEYLER, *Physiol. Chemie* Berlin 1877-81; LAACHE, *Die Anämie* Christiania 1883). It is highest at birth; in the first year it falls to one-half, and rises again between the fifth year and the forty-fifth to about two-thirds of its original amount; thence it again declines. Men have a somewhat higher proportion of hæmoglobin than women. The proportion diminishes during gestation. For methods of estimation, see GAMGEE (*Physiol. Chem.* I.); CORNIL and RANVIER (*Man. Path. Hist* I.); HART (*Quart. J micro. sci.* 1881); LYON and THOMA (*Virch. Arch.* vols. 84, 87).

MAAS has shown (*Deutsch. Zeitschr. f. Chir.* XVII.) that in animals rapid with-

drawal of water from the blood is followed by rapid diminution of blood-pressure and of temperature. He maintains that most cases of **sunstroke** or heat-stroke must be reckoned as cases of anhydræmia.

259. The changes in the blood discussed in the foregoing paragraphs have been merely quantitative. But there are also numerous **qualitative changes,** depending on the presence in the blood of foreign substances in solution. The chemical processes normally taking place in the blood are few and simple; the abnormal substances are thus either derived from the exterior, or are products of tissue-change abnormal in themselves or abnormally taken up into the blood; it is rare for abnormal substances to be generated in the blood itself. Most of these impurities of the blood are not traceable by means of the microscope; there are no histological tests for the presence in the blood of sugar, of urea, or of morphia. But few exceptions exist. Of the gases entering the blood by the lungs **carbonic oxide** produces the most striking change. It gives the blood a bright cherry-red color, which can often be recognized in the bright tint of the post-mortem *livores* or stains. On section the blood which flows from the vessels, and that contained in the parenchyma of the organs, alike exhibit the characteristic color. In cases of poisoning by **carbonic acid** the blood is dark, and the post-mortem stains violet or livid. The blood is likewise darkened, and may be even inky, after poisoning by **sulphuretted hydrogen.**

Of products of metabolism abnormally taken up into the blood, the salts of the biliary acids and the bile-pigments are most readily recognized. The **bile-pigments** color the plasma yellow. Probably the same effect may be produced by the biliary salts, for they bring about solution of the hæmoglobin and its transformation into bilirubin. The passage of bile into the blood is at once manifested by the yellow staining of the tissues, especially such as have no marked color of their own. This condition is known as **icterus,** or **jaundice.** If the staining is recent, the tint is yellow; after a time it passes into brown or grayish-green. The urine is likewise discolored, and the presence in it of the bile-pigments can readily be demonstrated by proper tests.

The plasma of the blood may be discolored by the presence of **methæmoglobin,** set free by the solution in it of the red corpuscles; the substance may be demonstrated in the blood, and also in the urine. If the quantity present is considerable the blood has a lake-red tint, while the urine may be stained from light brownish-red to a deep dark-red (Art. 262).

In what is called **uræmia,** a condition arising from impairment of the renal function, various matters accumulate in the blood which affect injuriously the several organs and especially the brain. The latter effect is indicated by the coma and convulsions which accompany the disorder. (CHRISTISON, *On granuar degeneration of the kidneys* Edinburgh 1839; SCHERER, *Verh. d. phys.-med. Gesell. zu Würzburg* II., VII.). In animals whose kidneys have been excised, urea

and various urinary extractives are found to gather in the blood. In **gout** the normal proportion of uric acid is remarkably increased (GARROD, *Med. chir. Trans.* 1848, and *Gout and Rheumatic gout* London 1876).

In acute yellow atrophy of the liver **leucin** and **tyrosin** have been detected in the blood. In some stages of diabetes the blood-serum becomes milky (**lipæmia**) from the presence of chyle or emulsified fat (HOPPE-SEYLER, *Physiol. Chemie;* GAMGEE, *Physiol. Chemistry* I.; SANDERS and HAMILTON, *Edin. med. Journ.* 1879).

CHAPTER IV.

CHANGES IN THE BLOOD-CORPUSCLES.

260. The formed elements of the blood, the red and white corpuscles, are not permanent structures; the red corpuscles are continually perishing while new ones take their place; and the white corpuscles are diminished in number by migration from the vessels, so that the proportion of them in circulation must be maintained by the development of new cells.

The number of white cells in the blood is not altogether constant even in health. It is now reckoned that on the average there is one white cell to six hundred red; but the proportion is often greater (as during digestion), and often less.

In many and various morbid conditions (as in continued suppuration, in typhus, typhoid, and intermittent fevers, in pyæmia, erysipelas, etc.) the white blood-cells are increased in number, multinuclear forms appearing as well as the uninuclear; the proportion may in such cases rise to 1 in 100, 1 in 50, or even 1 in 20. According to VIRCHOW the white corpuscles are most apt to be morbidly increased when the lymphatic glands are affected. The condition of morbid increase he calls **leucocytosis**; it is a temporary condition and dependent on transient causes.

Leukæmia (VIRCHOW) or **leucocythæmia** (HUGHES BENNETT) is to be distinguished from the merely temporary condition of leucocytosis. Its characters are—a more or less notable and abiding increase of white corpuscles, accompanied by a decrease of the red corpuscles. The proportion between the two may be so altered that their numbers become equal, or in extreme cases the white may slightly outnumber the red.

In well-marked leukæmia the blood is quite visibly altered in appearance; it looks pale, transparent, and limpid. *Post-mortem* the accumulations of white corpuscles may here and there be so great that they are apparent to the unaided eye. In the heart and great vessels peculiar muddy clots are found instead of the usual fibrinous deposits, or the ordinary post-mortem clots may be covered over with a white creamy pus-like film. The diagnosis of less-marked cases may require the aid of the microscope, by which even a slight relative increase of the white cells in the blood may be recognized.

Post-mortem examination of cases of leukæmia shows that changes in certain of the organs are associated with the changes in the blood; these

are no doubt partly cause and partly effect of the blood-changes. The hyperplasia of the spleen (Art. 328), of the lymphatic glands (Art. 344), and of the marrow of the bones, is considered as an originating factor of the blood-changes. The grayish infiltration which appears diffused or in patches through various organs like the liver, lungs, and kidneys, can scarcely be other than an effect; the white cells circulating in the blood have lodged and accumulated in the parts affected. These infiltrated cells lie partly within the vessels, and partly around them. Occasionally the appearances are such that we can only explain them by assuming that a **'white hæmorrhage'** or hæmorrhagic infarction has occurred. Besides these patches of simple infiltration tumor-like formations of lymphadenoid tissue are at times found in certain parts, such as the liver and kidneys.

BENNETT was the first to describe the affection, which he called leucocythæmia and regarded as a 'suppuration of the blood' (*Edin. med. and surg. Journ.* Oct. 1845; *Leucocythæmia* Edinburgh 1852; see also *Brit. for. med. chir. Review* 2, 1852). VIRCHOW recognized its true character and significance under the name of 'white blood' or leukæmia (*Froriep's Notizen* Nov. 1845; *Gesamm. Abhand.* p. 147).

The white corpuscles found in leukæmic blood are not all alike. A larger and a smaller variety can be distinguished, and in different cases one or another form may be the more abundant. VIRCHOW holds that the larger cells are derived from the spleen, and their abundance in the blood is due to a splenic hyperplasia; the smaller cells he traces to the lymphatic glands. From this point of view leukæmia has been characterized as splenic (lienal), lymphatic, or lymphatico-splenic, the latter form being intermediate between the other two. The relation of the spleen or lymphatic glands to the disease is thus assumed to be—that by the hyperplasia of these organs an increased supply of lymphoid elements is produced and conveyed into the blood. Attention has been called to the part played by the bone-marrow by the researches of BIZZOZERO (*Cent. f. d. med. Wiss.* 1869), NEUMANN (*Arch. d. Heilk.* XI., and *Berl. klin. Woch.* 6, 1879, with full references to other papers), PONFICK (*Virch. Arch.* vol. 67), WALDEYER (*Virch. Arch.* vol. 52), and others. In leukæmic patients the marrow often manifests very notable changes; it becomes yellowish and pus-like, and contains an excessive proportion of lymphoid cells. Going upon the assumption that lymphoid elements pass into the blood from the bone marrow as well as from the spleen and lymphatic glands, a fourth form of leukæmia has been described—the medullary or myelogenic form. This can seldom occur uncombined with other forms.

Nucleated red blood-cells have now and then been found in leukæmic blood (ERB, *Virch. Arch.* vol. 34; BOETTCHER, *ib.* vol. 36; KLEBS, *ib.* vol. 38; HAYEM, *Arch. de physiol.* 1883). NEUMANN (*Berl. klin. Woch.* 10, 1878) believes that this fact is sufficient to establish the participation of the marrow in the genesis of the affection; but BIZZOZERO and SALVIOLI (*Centralb. f. d. med. Wiss.* 1879) dispute this, and think the nucleated corpuscles are derived from the spleen.

It is impossible to assign definitely the parts taken by the different organs in the production of leukæmia. We do not even know for certain whether all the organs referred to are normally capable of contributing lymphoid elements to the blood. It still seems questionable whether the marrow takes the important share ascribed to it at all; it may well be that the accumulation of lymphoid elements observed in it is merely a secondary result of the general disease.

The ultimate cause of leukæmia is still unknown. It is not inconceivable that it may be due to a primary disorder of the substance of the blood itself (KOTTMANN, *Symptome der Leukämie* Berne 1877). LEUBE, PENZOLDT, and FLEISCHER have recently described cases (*Virch. Arch.* vol. 83, *Arch. f. klin. Med.* XXVI.) in which neither spleen nor lymphatic glands nor bone-marrow were affected; from this it would seem that structural changes in these tissues are not absolutely essential to leukæmia. Possibly, as KLEBS has suggested, it may in reality be an infective disorder.

It is a noteworthy fact that hyperplastic changes may take place in the spleen and lymphatic glands without any accompanying leukæmia. Such an affection is spoken of variously as malignant lymphoma, pseudoleukæmia, and lymphatic or splenic anæmia (Arts. 328, 344). The latter description refers to the fact that the affected patients gradually sink and die in extreme anæmia. Occasionally the pseudoleukæmia seems to pass into true leukæmia. Further details on the subject, together with full references to the literature bearing on it, are given by MOSLER in *Ziemssen's Cyclopædia*, Art. *Leukæmia*, vol. VIII.; also by FLEISCHER and PENZOLDT in *Arch. f. klin. Med.* XXVI., and by GOWERS, *Reynolds' Syst. of Med.* V. A peculiar feature of some cases of leukæmia is the presence in the blood of long needle-like octahedral crystals ('Charcot's crystals': CHARCOT and ROBIN, *Soc. de biol.* 1853, NEUMANN, *Arch. f. mikr. Anat.* II.; ZENKER, *Arch. f. klin. Med.* XVIII.; according to SCHREINER (*Liebig's Annal. d. Chem.* 1878) they consist of an organic phosphate).

EHRLICH has recently given much attention to the white blood-cells, and especially to their behavior with various staining-reagents (*Verh. d. physiol. Gesell. zu Berlin* 20, 1878–9 and *Zeitschr. f. klin. Med.* I.). He finds that a whole series of forms or stages can be distinguished. One form contains a single ovoid nucleus that stains feebly, another contains one or more rounded deeply-staining nuclei. Some cells show peculiar arrangements of their granules, whose power of taking up color varies in different cases. Others are notable for their power of absorbing eosin ('**eosinophilous cells**'). EHRLICH further notes that in all acute cases of leucocytosis the uninuclear and multinuclear cells are increased in number, but the eosinophilous cells are not. On the other hand when the hæmatopoietic organs are chronically diseased, as in leukæmia, the eosinophilous cells are increased in number. Compare SPILLING, *Blutuntersuch. bei Leukämie* In. Diss. Berlin 1880.

261. In speaking of the cases in which the whole amount of blood in the body is reduced, in other words of oligæmia, we mentioned that the number of the red corpuscles is simultaneously diminished. This condition, known as **oligocythæmia,** is recognized by the diminished proportion of hæmoglobin in the blood, and by the actual diminution in the number of red corpuscles contained in a drop of it. In extreme anæmia the number may fall to one-eighth or one-tenth of the normal. The diminution in the number of the corpuscles is often associated with changes in their form. Some of them are unusually minute and darker or lighter in color; they may measure 4–6 micromm. instead of 6–8 micromm. in diameter. This condition is referred to as **microcythæmia.** In some forms of anæmia, as in chlorosis and lead-poisoning, both abnormally small and abnormally large red corpuscles (microcytes and macrocytes) are found. Occasionally cells that are singularly altered in shape and

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corpuscles. Many of them crumble into fragments and dissolve (PONFICK, KLEBS); others, without being actually seen to break up, are rendered functionally useless and presently disappear. The products of disintegration circulate for a time in the blood, and are then at length eliminated.

Certain chemically-active substances act on the red corpuscles in the same way as high temperature; such are nitrobenzol (FILEHNE), potassium chlorate (MARCHAND), pyrogallic acid (NEISSER), sulphuric acid (LEYDEN and MUNK), nitrite of amyl (HOPPE-SEYLER), certain mushrooms of the morel kind (PONFICK), and the venom of certain serpents (HALFORD).

PONFICK has shown that when blood from one animal is transferred into the vessels of another the foreign red corpuscles become dissolved. In patients suffering from **intermittent hæmoglobinuria** LICHTHEIM showed that cooling of the cutaneous surfaces caused a great number of the red corpuscles to break up and dissolve in the plasma (Art. 259). Lastly in so-called **melanæmia**, a result of malarial infection, the blood-change is due to the destruction of the corpuscles and the retention of the disintegrated products in the blood. The effect is that the plasma contains granular pigment either free or enclosed in cells or agglomerated into irregular masses.

On the destruction of red corpuscles after burns see PONFICK (*Naturforscherversam.* Munich, 1877, *Berl. Klin. Woch.* 46, 1877), LESSER (*Virch. Arch.* vol. 79, with references), CATIANO (*Virch. Arch.* vol. 87), HOPPE-SEYLER (*Zeitschr. f. phys. Chem.* 1881), TAPPEINER (*Cent. f. d. med. Wiss.* 21 and 22, 1881). On paroxysmal or intermittent hæmoglobinuria see LICHTHEIM (*Samm. klin. Vorträge* 134, with full references), BOLLINGER (*Deutsch. Zeitschr. f. Thiermed.* III.), BOAS (*Arch. f. klin. Med.* XXXII.), ROSENBACH (*Berl. klin. Woch.* 10, 1880), EHRLICH. (*Deutsche med. Woch.* 16, 1881). On melanæmia see MOSLER (*Ziemssen's Cyclop.* VIII.), COLIN (*Traité des fièvres intermitt.* Paris 1870), Arnstein (*Virch. Arch.* vol. 61), KELSCH (*Arch. de physiol.* 1875). On the effect of transfusion see PONFICK (*Virch. Arch.* vol. 62). On poisoning with potassium chlorate see MARCHAND (*Virch. Arch.* vol. 77), and with mushrooms PONFICK (*Virch. Arch.* vol. 88) and BOSTRÖM (*Phys.-med. Gesell. zu Erlangen* 1880).

BIRCH-HIRSCHFELD (*Berl. klin. Woch.* 36, 1879) describes, under the name of epidemic hæmoglobinuria of infants, a disease observed by WINKEL in the Dresden Lying-in hospital; it attacked suckling children, who rapidly perished with symptoms of destructive change in the blood, cyanosis, jaundice, hæmoglobinuria, and petechial eruptions. Its cause is unknown.

CHAPTER V.

SOLID IMPURITIES IN THE BLOOD.

263. The morbid changes in the blood just discussed (Arts. 257–262) are all liable to produce more or less transitory pollution of the blood. Disintegrated corpuscles, such as are common after burns, can only be regarded as impurities which have to be eliminated; and so too the pigment-granules of melanæmia, and the crumbled fragments of softening thrombi, are matters foreign to healthy blood. They have this in common that they are the products of **morbid changes in the blood** itself. The minute groups of granules seen in some cases of anæmia are probably of the same nature; RIESS (*Reichert's Arch.* 1872) thinks they are disintegrated white cells, LEUBE (*Berl. klin. Woch.* 44, 1879) regards them as broken-down hæmatoblasts, BIZZOZERO (*Arch. ital. de Biologie* I.) as broken-down blood-plates.

Morbid changes in the vessel-wall may introduce impurities as well as changes in the blood itself. For instance, in some infective fevers the vascular endothelium becomes fatty and is shed into the blood-current. When the lining membrane of the heart or great vessels becomes inflamed it is not uncommon for fragments of diseased tissue to be swept off in like manner. Fatty or necrotic patches in the lining membrane are also very apt to contribute impurities to the blood; it is thus that fragments of necrosed valves, of inflammatory exudations, and of fatty detritus enter the circulation.

264. **Impurities derived from the tissues** are frequently conveyed by various channels into the blood. The lymphatic system is one channel, and solid matters may be taken up and carried along by the lymph-current directly. More commonly such matters are first taken up by contractile cells which act as carriers. Thus the products of disintegration of extravasated blood are carried off by corpuscle-carrying cells, and the products of fatty degeneration by fat-granule cells. In like manner other minute particles or even living tumor-cells may reach the blood.

But the lymphatics are not the only channel; it is not rare for the blood-vessels to be entered directly. A tubercle developed in the vessel-wall may break up, and be in part swept off by the current. Tumors, such as cancers, may likewise break into the vessels, and tumor-cells may be conveyed from them to remote points. Moreover, when vessels are

wounded extraneous organic matters such as fat may gain direct access to the blood, indeed after wounds involving adipose tissues the blood is almost always found to contain oil-globules.

265. **Extraneous corpuscular matters** may reach the blood in the same way as those derived from the tissues of the body itself. Inhaled coal-dust or steel-dust may pass through the pulmonary lymphatics and reach not only the glands but from them the blood itself, and similar minute solid matters may gain access directly from wounds. Here as before the migratory cells play an important part by taking up the foreign matters into their substance and carrying them to a distance. Of such foreign matters **animal and vegetable parasites** are unquestionably the most important. We have already discussed in the First Part the conditions under which such parasites gain an entrance. Their invasion of the blood is partly passive, and partly active. So far as it is passive the process is that just described; but many parasites have moreover the power of active penetration of the tissues, and so make direct avenues of entrance for themselves through the vessel-walls while they also use the pre-existing lymph-channels. It must also be remembered that many parasites, and chiefly the vegetable kinds, have the power of multiplication within the blood; so that every drop may contain a multitude of individual organisms. The best examples of this are afforded by the anthrax-bacillus and the spirillum of relapsing fever. In the case of the other bacterial affections this process of multiplication within the blood has not yet been demonstrated, though there are many disorders in which brood-colonies are met with in the smaller blood-vessels, as in pyæmia (Art. 199). Among animal parasites the *Filaria sanguinis* (Art. 235) is the only one which occurs in great numbers in human blood. Trichinæ, when they do enter the blood, stay only a short time in it. As to the seat of the *Distoma hæmatobium* or *Bilharzia* see Art. 239; and for *Echinococcus* see Art. 248.

The **entrance of air** into the blood-vessels deserves special mention. It most frequently results from wounds of the great veins in the neighborhood of the thorax; but it may also occur in consequence of ulceration into the veins, as in cases of gastric ulcer (JÜRGENSEN), or after parturition through the open uterine sinuses. If not rapidly absorbed the bubbles of air behave like small solid bodies and produce like results.

266. It may be taken as a general law that no foreign body can for any long time remain in the blood; it is either deposited, or destroyed, or eliminated from the circulation. It may be deposited in very various localities; a large body will naturally lodge in the heart or a great vessel, a smaller one may pass into a capillary.

If a large quantity of **air** enters the right heart from a venous trunk, it forms with the blood a bulky froth, which the contractions of the heart are unable to propel effectively. The result is that little or no blood reaches the left heart, the blood pressure in the aorta sinks, and

the patient quickly dies. If, however, the quantity of air which enters the blood is small, or its entrance slow, it is carried on in the form of minute bubbles, and may circulate throughout the body. Larger quantities may produce local disturbances of the circulation, and so interfere with the cerebral or respiratory functions, but after a time it is all absorbed.

Small bodies such as **fat globules** or **pigment granules** generally lodge in the capillaries of the various parts. Certain organs seem to be favorite seats for such lodgments; such are in especial the spleen and liver, and frequently also the kidneys and bone-marrow. The observation may often be verified on the post-mortem table, but it may also be experimentally demonstrated (PONFICK). The cause of the preference for these organs probably lies in their anatomical structure, in consequence of which the blood-current through them is unusually slow. As regards the spleen, an additional factor comes into play in the permeability of its vessel-walls; this specially favors the extravasation of small bodies from the blood-current, and in particular such as are inclosed in contractile carrier-cells.

The process of deposition is most easily followed in the case of pigmentary matters, such as disintegrated blood, or iron-compounds, or granular coloring matters inhaled or injected into the blood. The spleen pulp may in such cases become deeply stained, and sections of the liver may also show the effect in a very instructive manner. In the latter instance the deposit lies chiefly around the periphery of the lobules. At first the foreign matters are seen to lie within the vessels, but afterwards they partly pass out of them into the tissues. This escape is generally effected by the help of contractile carrier-cells (Arts. 112–114), but free corpuscular matters may escape from the capillaries directly, especially from those of the spleen.

The behavior of **bacteria** in the vascular system has already been discussed (Arts. 199–200). The embolic occlusion of arteries by larger foreign bodies, and its results, are described in Arts. 29, 33, and 255–257.

The fate of foreign bodies which have gained access to the blood has been the subject of several experimental researches by PONFICK (*Virch. Arch.* vol. 48), SLAVJANSKY (*ibid.*), RUPPERT (*Virch. Arch.* vol. 72), SOYKA (*Prag. med. Woch.* 1878), and others. Cinnabar, or coal-dust, or Chinese black was introduced into the blood of animals, either directly, or through the pulmonary lymphatics by inhalation. These substances were found to become inclosed in contractile cells, and to be deposited outside the vessels in the spleen, liver, kidneys, and bone-marrow. The carrier-cells generally take up the foreign matters before they leave the blood; but in the spleen pulp and in the marrow they may become enclosed after escaping.

On the subject of **fat-embolism** see SCRIBA (*Deutsch. Zeitschr. f. Chir.* XII., with full references), FLOURNOY (*Contrib. à l'étude de l'embolie graisseuse* Strasburg 1878), HAMILTON (*Edinburgh Med. Journ.* 1879), JOLLY (*Arch. f. Psych.* XI.), JACOBSON (*Holmes' Syst. of Surg.* I.), MANSELL-MOULLIN (*Inter. Encyc. of Surg.* I.).

On the consequences of the entrance of air into the blood-vessels, JÜRGENSEN has recently published (*Arch. f. klin. Med.* XXXI.) the results of his clinical and experimental investigations; they partly bear out and partly extend the results previously obtained by BICHAT, MAGENDIE, MURON, LABORDE, COUTY, and others. He states that air injected distally into the right femoral artery appears after thirteen minutes in the left femoral vein, having passed through three capillary systems. The air may continue to circulate for hours, but is ultimately absorbed. When air enters the pulmonary vessels, dyspnœa with brief respiratory pauses is induced. When life is in danger, the respiration is notably slowed. So long as air is in circulation the proportion of oxygen in the blood is diminished.

267. The **ultimate fate of foreign substances** which have been arrested in the blood-vessels or have passed into the neighboring tissues, varies according as the substances are destructible or not.

Insoluble matters, like cinnabar, coal-dust, etc., remain in the tissues permanently, or are in part eliminated from the body. Experiment shows that after many weeks some part of the substance may still lie enclosed in cells within the tissues. During this time some movement of the substance always takes place; the carrier-cells change their position, and may even enter the blood once more. In this way part of the substance is carried to the exterior of the body, and that by various routes. In the first place, glands like the kidneys, liver, or mamma, whose secretion passes out of the body, may eliminate the foreign substance with the secretion. But it may also pass out through the mucous membranes, through the lungs, through wounded parts, or even through the skin; such is especially the case when active cell-migration is taking place at any of these sites. For example, if we introduce a considerable amount of insoluble coloring matter into the blood or lymph of an animal, and then induce inflammation at any point, a large proportion of the migratory leucocytes will be found to have portions of the coloring matter inclosed in their protoplasm. In spite, however, of these processes, by which the organism gets rid of its impurities, some part of the foreign substance will usually remain in the tissues; and if the substance is colored, a morbid or abnormal pigmentation of the organs may result.

Many of the extraneous substances entering the blood are soluble and destructible, and such always disappear after a longer or shorter time. Thus inhaled particles of chalk-dust are dissolved in the blood; fat, which circulates in great drops, rapidly disappears; and micro-organisms likewise break up and are absorbed, so soon as they cease to find the vital conditions that are necessary to them. Even embolic plugs of considerable size (such as fragments of thrombi, of diseased valves, etc.), are in time dissolved and disappear (see Arts. 114–115 and 254–257, where the effects of septic or infective embolism are described).

Emboli consisting of living cells may proceed to grow and develop at the spot where they lodge. This happens, for example, in the development of secondary tumors (Art. 174).

268. The question as to **what becomes of disintegrated red cor-**

puscles has a special interest. We have already said in Art. 260 that the lifetime of a red corpuscle is but brief; according to QUINCKE (*Deutsch. Arch. f. klin. Med.* XXVII.) it is probably not longer than two or three weeks. At the end of that time it becomes functionally inactive, is taken up by the white cells, and eliminated from the blood. QUINCKE says this happens chiefly in the liver and spleen, possibly also in the bone-marrow. The red corpuscles and their *débris* inclosed in the white cells of the spleen-pulp are transformed into colored or colorless ferro-albuminoid compounds, which may be micro-chemically demonstrated either in the soluble or the granular form. From the spleen and marrow, perhaps also from the liver, some part of these iron-compounds passes again into the blood, being utilized in the formation of new red corpuscles; the remainder is excreted by the liver-cells.

If however the destruction of blood-cells becomes so excessive that hæmoglobin appears in solution in the plasma, the kidneys take part in the eliminating process, and **hæmoglobinuria** is induced. Hæmatogenous and biliary pigments which have passed into the blood (as from old hæmorrhagic patches, for example) are excreted in the urine as urobilin (KUNKEL, *Virch. Arch.* vol. 79). The more insoluble parts of the red corpuscles reach the spleen, liver, and bone-marrow; and there the normal process of disintegration becomes intensified so as to meet the demand on it thus occasioned. In these organs numbers of cells can be seen which contain fragments of red corpuscles, or brown and yellow flakes and granules of pigment; and similar flakes and granules also occur free. The pigmentation of the organs may in this way become very intense. The kidneys also generally contain fragments of pigment in the glomeruli, tubules, and interstitial tissue. PONFICK has pointed out (*Berl. klin. Woch.* 1877) that such deposits are often associated with serious textural and functional changes in the kidneys, and especially with the formation of tube-casts and fatty degeneration of the renal epithelium.

The brown flakes and granules found in these deposits have not always the same composition. They are in part proximate derivatives of the blood-pigments such as bilirubin and hæmatoidin, formed directly from hæmoglobin; partly ferro-albuminoid bodies (QUINCKE); and partly other compounds of iron such as the hydrated sesquioxide (KUNKEL, *Virch. Arch.* vol. 81).

The liver and spleen may be unable to deal with the increased amount of material brought to them when the disintegration of corpuscles in the blood exceeds a certain limit; that is to say, they may not be able to destroy it or to eliminate it with the bile. Hence these organs may show signs of more or less temporary pigmentation or of deposits of iron-compounds (QUINCKE, KUNKEL); and the same is occasionally seen in other organs. Part of the iron deposited may possibly be derived directly from dissolved hæmoglobin which has not undergone change in the interior of carrier-cells.

QUINCKE moreover affirms that such deposits of iron may occur when from any cause the formation of new corpuscles is interfered with. The iron-compounds naturally formed are not utilized speedily enough in forming blood, and are not at once eliminated from the body.

The above account of the formation of pigment-granules containing iron rests mainly on the researches of QUINCKE and KUNKEL. It is to a certain extent confirmed by the case described by HINDENLANG (*Virch. Arch.* vol. 79), in which pigmentary infiltration of many of the organs was observed in a patient dead of purpura, in whom a large extravasation of blood had undergone absorption. The liver, spleen, pancreas, kidneys, and other organs contained yellowish-brown pigment-carrying cells, and yellow and brown flakes and granules of free pigment. KUNKEL examined the pigment and found it to consist of hydrated ferric oxide with a mere trace of hæmatin; while, as ZIEGLER convinced himself, the appearances were exactly those of the pigmentary infiltrations found in other like cases. It may therefore be granted that in such cases pigments may be formed containing iron, which are not at all or only remotely related to hæmatin (Art. 68). QUINCKE, who demonstrated by chemical tests the presence of iron in pigmented sections, found it occurring diffused or as minute granules in the lymphatic glands, liver, and kidneys. He calls the condition **siderosis**, a term that is in itself not inapt, though it has already been applied to the deposit of inhaled steel-dust in the lungs.

CHAPTER VI.

CHANGES IN THE LYMPH.

269. The **lymph** is merely the liquid transuded from the blood-vessels, together with certain products of tissue-metabolism and certain matters taken up (*e. g.* by the lacteals) from the outside. To this the lymphatic glands contribute a number of lymphoid elements, in addition to the few cells derived from the blood. The sources of

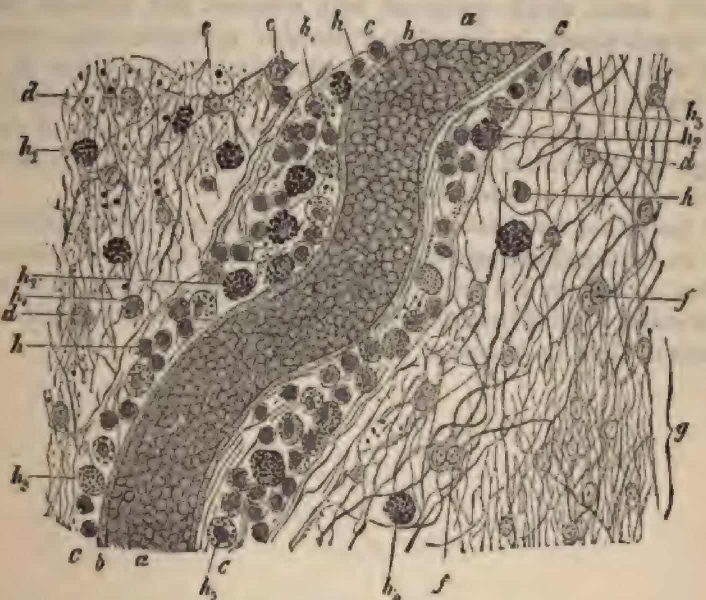


FIG. 120. SECTION THROUGH A DEGENERATING PATCH FROM THE BRAIN.

(*Perosmic acid preparation:* × 200).

a, blood-vessel filled with blood.
b, tunica media.
c, adventitia with its lymph-sheath.
d, unaltered neuroglia-cells.
e, fatty neuroglia-cells.
f, binuclear neuroglia-cells.
g, sclerosed tissue.
h, lymphoid cells.
h_1, lymphoid cells containing a few oil-globules.
h_2, fat-granule carriers.
h_3, pigment-granule cells, some containing red corpuscles.

the lymph being thus somewhat various, we may expect that morbid changes in its composition will not be uncommon. Changes in the blood

and disorders of the tissues generally give rise to changes in the lymph; and the various impurities of the blood already described are all of them apt to pass into the lymphatic system on leaving the blood-vessels. To discuss in detail the changes which may take place in the lymph would in fact require us to repeat what we have said concerning the impurities of the blood, as well as to go through all the morbid processes affecting the tissues in which the lymph-stream takes its rise.

Many of the changes referred to are not capable of microscopical demonstration, being due to substances dissolved in the lymph. As regards the formed elements, the morbid changes are either such as to relate to the quantity or quality of the lymph-cells, or to the addition of solid products of tissue-waste or of foreign matters derived from without. As an example of such changes in the normal contents of the lymph, we may refer to Fig. 120, representing a perivascular lymph-sheath (c) from a lunatic's brain, which contained both sclerosed and softened patches. The lymph-sheath is dilated and contains numerous cells, which are laden with colorless products of degeneration of brain-tissue (h_1 h_2), or with the *débris* of disintegrated blood (h_3). There are also lymphoid cells (h) not inclosing any such matters. The two former kinds of cells are foreign to the normal lymph of the brain, and even of the latter the numbers are here abnormally great.

A lymphatic vessel taken from tissue in a state of inflammation would show an abnormal increase of cellular elements in the lymph it contained; another taken from the neighborhood of a tumor would probably contain tumor-cells; a third from a region invaded by micrococci would contain colonies of these in process of development, and so on.

SECTION II.

THE VASCULAR MECHANISM.

CHAPTER VII.

MALFORMATIONS AND MALPOSITIONS OF THE HEART.

270. The development of the heart is so complex, and so dependent on the accurate co-ordination of many diverse stages and processes of growth, that its liability to malformation is not surprising. The chief abnormalities which occur are—insufficient size of the heart as a whole, and defective development of the septa and of the ostia. These are often associated with defects in the large vessels.

The **defects in the septa** may vary from the entire absence of any partition to the persistence of minute openings which have no effect whatever on the functions of the heart. The commonest defects are—patency of the foramen ovale, and deficiency of the ventricular septum beneath the aortic valves.

Defects of the ostia are generally of the nature of valvular deformities. Some of these are unimportant unless they interfere with the competency of the valves; such are excess or diminution in the number of valvular segments, and slighter anomalies in their form or relative position. When the malformation of the valves is such as to interfere with their functions by causing incompetency or stenosis, the case is more serious, and may become extremely serious. Many of the commoner valvular malformations, especially such as are of the nature of thickening, contraction, or adhesion, are referable to inflammatory affections *in utero*. Occasionally traces of such inflammations are to be found elsewhere than about the valves, and generally in the form of whitish thickenings on the surface of the endocardium (Arts. 281–283).

Development of the heart. The heart is originally formed out of two lateral mesoblastic tubes which coalesce into an undivided straight tube. This single tube is continuous in front with the two primitive aortas, and posteriorly it receives the two vitelline veins from the vascular area. In consequence of the continued growth of the single tube it becomes doubled on itself into an S-shaped structure, and presently by slight constrictions three somewhat sacculated sections can be made out. The anterior almost straight section is the aortic bulb; the middle section has somewhat thickened walls and forms the ventricular portion; the posterior section is thin-walled and forms the auricular portion.

By the continued bulging and growth of the ventricular portion the aortic bulb and the auricular portion are brought into approximate juxtaposition, and sometimes seem to twist round each other. The ventral bulge of the ventricular portion indicates the position of the future apex.

The next step is the separation of the ventricular portion into two chambers. This begins to take place about the seventh week by the development of a low crescentic fold from the inner surface of the right wall below, while an evanescent notch appears at the corresponding spot outside. The fold grows rapidly upwards towards the auriculo-ventricular opening, where it is in relation both with the auricular portion and the aortic bulb. For a time therefore communication between the ventricles is free over the top of the septal fold.

The septum of the auricles begins to appear about the eighth week as a low crescentic fold, starting from the anterior wall of the auricular portion and the upper edge of the ventricular septum. In the tenth or eleventh week two other folds grow up from the posterior wall, one coming forward to meet without adhering to the anterior fold, and forming the valve of the foramen ovale; the other fold is the Eustachian valve. The auricular septum thus remains incomplete until after birth, when the valve usually coalesces with the margin of the foramen ovale, and the latter ceases to be patent.

The division of the arterial bulb begins, about the seventh week, by the development of an internal septum proceeding from the distal end towards the ventricles. Two channels are thus formed from the single cavity, and the direction of the septum twists in such a way that the anterior channel (pulmonary artery) becomes continuous with the cavity of the right ventricle, and the posterior channel (aorta) with the cavity of the left ventricle. The septum ultimately meets and joins the septum of the ventricles.

The two primitive aortas form the first or primitive pair of aortic arches and converge dorsally and posteriorly to form a single trunk. Between the ascending and descending limbs of each arch are developed four secondary aortic arches, while the primitive arches almost entirely disappear. The great arterial trunks are derived chiefly from the three lower secondary arches, but portions of the primitive and of the highest secondary arches persist in the internal and external carotids.

271. **Defects** of development **in the large arterial and venous trunks** are of grave import. Such defects are very much more frequent in the arteries than in the veins. Thus we may have absence or imperfection of the septum of the aortic bulb, so that the aorta and pulmonary artery rise from a single stem. Or the position of the septum may be abnormal, whereby the aorta is displaced to the right; in extreme cases it may even arise from the right ventricle.

Of the vessels which are not directly connected with the heart the most interesting is the **ductus arteriosus** (*ductus Botalli*), which unites the pulmonary artery with the descending aorta. It naturally becomes occluded and impervious after birth, but in many cases it remains patent, especially when defects in the aorta or pulmonary artery make its persistence necessary to life. This happens notably in cases of atresia of either trunk; if blood is to reach the branches at all it must pass from the pervious trunk through the ductus into the other.

It is always to be remembered in connection with this subject that many of the miner anomalies are merely the necessary results of other more fundamental malformations. Thus the malposition of the septum of the aortic bulb may involve the displacement of the aorta to the right (ROKITANSKY), and there may in consequence be a defect in the ven-

tricular septum, even though it is sufficiently developed to have met the septum of the bulb had the conditions been normal. Similarly a primary defect in the ventricular septum may lead to secondary deformities elsewhere (ORTH). If the right auriculo-ventricular orifice should be narrowed or closed, the blood from the right auricle must pass into the left auricle; and this will naturally prevent the closure of the auricular septum. And so generally, a defect at one point is to a certain extent compensated for by a corresponding abnormality at another. Not infrequently the connected series of malformations is highly complex, so that it is not always easy to make out their mutual relations.

Summing up we may say, that the **causes of cardiac malformations** are to be sought either in lack of developmental energy, or in imperfect co-ordination of the several stages and processes of growth, or in inflammatory disease attacking the heart *in utero*.

According to FÖRSTER the chief forms of cardiac malformation are the following.

(1) Absence or deficiency of the septum of the aortic bulb, with deficiency of the other septa; of this there are various degrees:—

(*a*) the heart is in two parts, one corresponding to the ventricular portion and the other to the auricular portion

(*b*) the heart has two auricles and one ventricle.

(2) Atresia or stenosis of the aorta or pulmonary artery, with partial deficiency of the septa:—

(*a*) aorta narrow or impervious; pulmonary artery conveys blood to the aorta and its branches through the ductus arteriosus; auricular and often ventricular septum imperfect; left ventricle ill-developed, right ventricle large

(*b*) pulmonary orifice narrow or impervious; lungs supplied with blood from the aorta through the ductus arteriosus; auricular and ventricular septa generally imperfect, the latter may be closed; this form is not infrequently met with in clinical practice.

(3) Defective metamorphosis of the arterial arches:—

(*a*) stenosis of the aortic arch above the entrance of the ductus arteriosus; the latter remains patent and conveys blood from the pulmonary artery to the descending aorta

(*b*) transposition of the great trunks; aorta rising from the right, pulmonary artery from the left ventricle; septa deficient; more rarely the great veins are likewise transposed

(*c*) aorta and pulmonary artery both rise from the right ventricle.

(4) Patency of fœtal apertures, the arteries being normal.

The commonest example is offered by the foramen ovale; minor deficiences in the auricular septum have no effect on the circulation. The ductus arteriosus may remain open for a long time; if the channel be narrow its patency has no importance. Minor deficiencies in the ventricular septum are less common; they may become of importance if the function of the heart is impaired from other causes.

(5) Atresia or stenosis of an auriculo-ventricular orifice.

Here the auricle may be shut off from the corresponding ventricle; the septa are always deficient.

(6) Deformity of the valves.

The valves may be stunted, morbidly adherent, misshapen, or abnormally subdivided in a multitude of ways; the result may be incompetence or stenosis.

The malformations above described are often incompatible with life. In other cases life is possible but the circulation is gravely disordered, which may be indicated during life by extreme cyanosis.

References:—FÖRSTER, *Handb. d. path. Anat.* and *Die Missbildungen des Menschen* Jena 1865; PEACOCK, *Malformations of the human heart* London 1866 (with references to the earlier literature); MAIER, *Allg. path. Anat.*; ROKITANSKY *Die Defecte d. Scheidewände d. Herzens* Vienna 1875; ORTH, *Virch. Arch.* vol. 82; ASSMUS, *Deutsch. Arch. f. klin. Med.* XX.; REIL, *ibid.* XVII.; RAUCHFUSS, *Gerhardt's Handb. d. Kinderkrankh.* vol. IV. Tübingen 1878; TARUFFI, *Sulle mal. congenit. d. cuore* Bologna 1875; GREENFIELD, *Trans. Path. Soc.* XXVII. (1876); BUHL, *Zeitschr. f. Biologie* XVI.; LORENZ, *Wien. med. Jahrb.* 1880; ORTH, *Virch. Arch.* vol. 82, and *Lehrb. d. spec. path. Anat.* vol. I. Berlin 1883; DILG, *Virch. Arch.* vol. 91.

272. It is not rare for the heart to be abnormally small in proportion to the body-weight. The condition is described as **cardiac hypoplasia**. The heart is either abnormally small at birth, or it simply lags behind the body in its growth. Thus in adults the heart may be no bigger than it normally is in children of seven or eight. Such extreme cases are rare, but minor degrees are often met with. VIRCHOW showed that cardiac hypoplasia is common in patients suffering from chlorosis or hæmophilia. The aorta and arteries in such patients are usually narrow and thin-walled; while the genital organs, and sometimes the entire body, are ill-developed. General hypoplasia of the vascular system occurs in men as well as in women. As the growth of the heart is in a measure conditioned by the work it has to do, the increased resistance caused by the narrowness of the aorta may bring about a compensatory or functional hypertrophy of the heart muscle.

The abnormal thinness and narrowness of the great arteries are often associated with anomalies in their distribution; and corrugated or lattice-like irregularities of surface are also observed on the inner coat of the aorta. In such cases the aorta is peculiarly liable to fatty change, and to spontaneous rupture.

The heart may be misplaced in the thorax; the most notable case being that of transposition or **dexiocardia**. This is rarely a solitary malposition (KRIEGER, *Ueb. reine Dexiocardie* In. Diss. Berlin 1880), it is nearly always part of a general *Situs inversus* (Art. 11).

In cases of fissural malformation of the wall of the thorax and abdomen (Art. 9) the heart is not uncommonly displaced forwards (*Ectopia cordis*). The pericardium may be present or absent; but total or partial absence of the pericardium without other malformation is very rare.

References on the size of the heart and blood-vessels in normal and morbid conditions:—PEACOCK, *On the size and weight of the heart* London 1854; VIRCHOW, *Ueb. die Chlorose u. die damit verbundenen Anomal. am Gefässapparate* Berlin 1872; BAMBERGER, *Lehrb. d. Krank. d. Herzens* Vienna 1857; BENEKE, *Die anatom. Grundlagen der Constitutions-anomalieen* Marburg 1878; BUHL,

Mitth. a. d. path. Inst. zu München Stuttgart 1878; DU CASTEL, *Arch. gén. de méd.* 1880; SPATZ, *Arch. f. klin. Med.* xxx.; THOMA, *Unters. üb. d. Grösse u. d. Gewicht d. anat. Bestandtheile d. mensch. Körpers* Leipzig 1882 (with full references and very accurate measurements); MÜLLER, *Die Massenverhältnisse d. menschlichen Herzens* Hamburg 1883 (with elaborate tables).

According to BENEKE the volume of the heart in new-born infants is 20–25 ccm.; when its development is complete 215–290 ccm.; in the prime of life 260–310 ccm. In cases of hypoplasia the volume may be reduced by a third or more.

CHAPTER VIII.

ATROPHY AND DEGENERATION OF THE HEART.

273. **Simple brown atrophy.** In patients who have died of general marasmus the heart is often found to be greatly reduced in size. The investing fat is almost or altogether transformed into a gelatinous or mucoid substance, occasionally stained with yellowish pigment. The superficial cardiac vessels lying under the visceral pericardium are much convoluted from the shrinking of the subjacent structures; the cavities are small; and the muscular walls are thinned. They are also firmer than normal, and stained of a brownish tint. The endocardium is apparently thickened, but this is due to its enforced adaptation to a smaller surface than it originally covered. Indeed in simple cases the muscle-cells are the only elements which are altered (Fig. 121). The muscle-cells are abnormally small, and contain numerous fine yellow pigment-granules lying chiefly at the poles of the nuclei, but also scattered through the protoplasm of the cells. These retain their normal striation. If it were necessary we might distinguish some cases as exhibiting simple pigmentary atrophy, and others brown pigmentary atrophy, according to the amount of pigment present. Brown atrophy is not infrequently associated with fatty degeneration of the heart.

FIG. 121. BROWN ATROPHY OF THE MUSCLES OF THE HEART.
(*Teased preparation:* $\times 350$.)

274. **Fatty degeneration and cloudy swelling.** Fatty degeneration is one of the commonest affections of the substance of the heart and not infrequently a cause of death. It is either uniformly diffused over the heart-muscle, or concentrated at certain spots. In the former case if the affection is at all advanced the muscular substance appears pale, yellow, limp, and easily torn; in the latter case it is speckled or mottled. The mottling is most beautifully seen in the papillary muscles and the trabeculæ of the right heart; the delicate and often regular yellowish streaks recalling the grain of some fine cabinet wood. Less intense degrees of fatty change are indicated by simple yellowish discoloration; but certainty of diagnosis is often only to be attained by the aid of the microscope. A fatty muscle-cell is interspersed with minute colorless dark-bordered oil-globules, whose number varies much according to the degree of degene-

ration which exists. At times they are so numerous that both nucleus and striation are overlaid and disappear. But even in such extreme cases the globules do not coalesce into large drops.

FIG. 122. FATTY DEGENERATION OF THE MUSCLES OF THE HEART (× 350).

Fatty degeneration of the heart is usually very gradual in its onset. It is most commonly a result of valvular lesions, pulmonary emphysema, or general anæmia, that is to say of disorders involving malnutrition of the heart-substance. According to EICHHORST (*Die troph. Beziehungen d. Nerv. vagus z. Herzmuskel* Berlin 1879) section of the vagi is followed by fatty degeneration of the heart. Acute fatty change is likewise observed in the course of infective and toxic affections. In such cases a stage of cloudy degeneration (Art. 48) precedes the fatty change, the muscular fibres assuming a peculiar grayish-yellow tint and a dull fish-like lustre. The muscle-cells look as if powdered, and contain fine albuminous granules which disappear when treated with acetic acid. In the later stages fat-globules appear. If the fatty degeneration of the heart is extreme it may lead to rupture of its walls, and so to fatal hæmorrhage.

275. **Fatty degeneration of the endocardium** is to be distinguished from the like change in the heart-muscle. It appears in the form of circumscribed patches of an opaque white color. The connective-tissue cells of the intima (Fig. 123) are found to be filled with larger or smaller oil-globules. These patches are most commonly seen on the valves, and especially the mitral valve. They may be quite small, or may cover the greater part of the valve. They usually occur in aged persons, whose vascular system elsewhere shows signs of analogous change. But they may also be found in younger persons, and even in children, especially such as have died of general marasmus or anæmia, or from some imperfection of development in the vascular system.

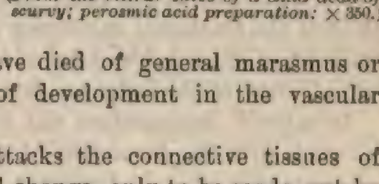


FIG. 123. SECTION OF FATTY ENDOCARDIUM. (*From the mitral valve of a child dead of scurvy; perosmic acid preparation:* × 350.)

Amyloid degeneration likewise attacks the connective tissues of the heart. A slight amount of amyloid change, only to be made out by proper reagents under the microscope, is not uncommon and may occur in any part of the heart-wall. Well-marked change recognizable by the naked eye is rare. When it occurs (Art. 59), and extends to the fibrous tissues of the endocardium, myocardium, and pericardium, these become remarkably thickened. The thickening may be uniform and smooth surfaced, or it may be irregular and nodular; so that, for example, the surfaces of the valves may become remarkably rough and granular. Within the heart-wall the amyloid tissue forms patches and swathes and

bands, between which the muscular tissue is apt to atrophy. The amyloid tissue is distinguished from the ordinary fibrous tissue by its greater translucency and firmness. Where the fibrous tissue is vascular, the amyloid change is particularly apt to attack the walls of the vessels.

276. **Hyaline and mucoid degeneration of the endocardium** is very common. It may almost be regarded as a physiological change accompanying old age, when the endocardium, especially that covering the valves, undergoes a certain amount of thickening; it merely implies an increase of connective tissue. But it not infrequently takes place in an irregular manner, leading to the formation of flattened or nodular or even pectiniform prominences on the surface. Such growths are chiefly found near the free edges of the valves, but they also occur at their bases and on the tendinous cords. The *corpora Arantii* of the aortic valves are very apt to be thickened in this way.

A certain amount of textural change is usually associated with the thickening of the tissues. The fibrous texture is gradually lost and the tissue becomes homogeneous, while the nuclei dwindle and disappear. This homogeneous or hyaline change with thickening somewhat resembles amyloid degeneration; but it may appear simultaneously with the latter, it generally occurs under altogether distinct conditions, and it gives no reaction with iodine.

The homogeneous degeneration may ultimately lead to necrosis of the affected tissue, which thereupon becomes turbid and breaks up into granular detritus. Not infrequently fat is formed in the tissue before necrosis sets in; and calcareous salts may likewise be deposited. Such changes are included under the term **atheroma.** The affected spots have first a dull white look, but when calcareous deposits have been made the tissue becomes hard and rigid and of a brilliant white color.

As a sequel to homogeneous degeneration in old age, or at times independently of it, we may have mucoid degeneration. The tissue assumes a clear jelly-like appearance, readily distinguishable from the brilliant white of the thickened calcareous patches. The change occurs in spots, generally in the neighborhood of the mitral and aortic valves; the *corpora Arantii* of the latter are favorite sites.

In mucoid degeneration the ground substance of the tissue becomes liquefied, with the formation of mucin. In extreme cases the ground-substance may entirely disappear. Fatty and calcareous change is often associated with the mucoid change.

Inflammatory processes are very apt to be set up in connection with the various degenerations described in this Article, and with the necrosis which they frequently induce. Such processes lead to infiltration of leucocytes around the foci of degeneration; and in this way new fibrous tissues may occasionally be formed.

277. **Myomalacia cordis** is the name given to a peculiar softening of the muscles of the heart, consequent on arterial anæmia (ischæmia).

The commonest cause of such anæmia is disease (such as sclerosis or atheroma) of the nutrient arteries of the heart, the coronary arteries and their branches; more rarely it may be due to coronary embolism.

The softened spots have different appearances according to their age and the amount of blood they contain. When the softening is recent, the spots are pale yellow and the tissue soft and fragile; sometimes the cut surface of a cross-section sinks in so as to become concave. If in consequence of the occlusion of an artery there has been an extravasation of blood from the capillaries, so that an infarct is produced, the softened patch becomes uniformly dark-red, or else mottled with red, brown, and yellow. After a time it turns grayish-yellow or rusty brown, and ultimately a translucent gray. Such patches are oftenest found in the wall of the left ventricle, especially near the apex; but they also occur elsewhere, as in the right ventricle. The papillary muscles may likewise undergo localized softening; or the entire muscle may be transformed into a grayish-yellow or semi-translucent mass. If the softening reach the endocardium thrombi (taking the form of cardiac polypi) may be formed over the spot.

When the softening is so extensive as to include almost the entire thickness of the heart-wall, rupture of the heart will result, and blood escapes into the pericardial sac. The rent is generally irregularly serrated, and is seldom large.

The tissue-changes underlying the varying appearances of the softened patches are partly retrogressive and partly constructive. The original ischæmia first of all brings about the destruction of numbers of muscle-cells. In the yellowish patches the muscular fibres are in various stages of degeneration and disintegration. This can be demonstrated in teased preparations, in which irregular fragments of muscle-cells and masses of granular detritus are seen. Generally some formation of oil-globules has also taken place. Sections of the muscular wall show the destructive process even better than do the teased preparations. Fig. 124 represents a section through a degenerating muscular bundle. In the upper part the muscle-cells are still unaltered and present the ordinary appearance (*a*). In the middle the cells (*b*) are beginning to break up into fragments, while below (*c*) they are completely disintegrated into granular detritus. The destruction is often limited to the muscle-cells, but at times the connective tissue likewise suffers; in such cases the nuclei cease to take up color when the section is stained (*d*), and granules are deposited among the pale fibrils of the connective tissue.

When hæmorrhage occurs as an accompaniment, we may find entire or fragmentary blood-cells mingled with the connective tissue and in part replacing the disintegrated muscle-cells; and in later stages the tissue will contain pigment-granules.

When the destructive process has gone a certain length, and death does not ensue, processes of repair are set up. The detritus is re-absorbed

and carried off, and the gap filled up by scar-tissue. Migratory leucocytes pass out of the vessels, and reactive inflammation begins. The detritus is for the most part taken up by these migratory cells, in part also taken up by the vessels directly or in solution. Ultimately fibrous tissue develops from the granulation-tissue built up by the leucocytes and perhaps by the multiplication of the fixed tissue-cells of the surrounding parts; but the muscle-cells are not reproduced. After a time the affected area is thus filled up with fibrous tissue containing a certain number of cells in its meshes. The muscle-cells which survive lie embedded in the new-formed tissue; and if hæmorrhage has occurred the tissue will also contain flakes and granules of pigment.

To the unaided eye the presence of the scar-tissue is manifested by its

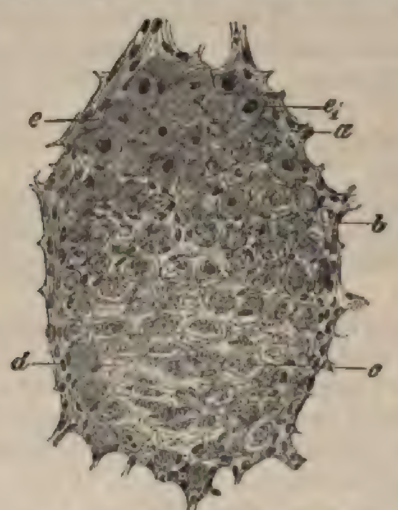


FIG. 124. *MYOMALACIA CORDIS.*

(Section through a degenerating muscular bundle: double staining with hæmatoxylin and carmine: × 300.)

a, normal muscle-cell.
b, disintegrating muscle-cell.
c, completely degenerate muscle-cell resolved into granular detritus.
d, non-nuclear fibrous tissue.
e, normal nucleus of muscle-cell.
e_1, swollen nucleus.

grayish translucent look when recent, and its glistening white color when more mature; the scar moreover seems to ramify through the muscular substance. Such scars are referred to as fibroid indurations or **scleroses of the heart,** and may thus represent the last stage of a localized softening. The bulk of the scar is usually less than that of the muscle it replaces, so that the heart-wall is abnormally thin at the affected spot (Art. 285).

Myomalacia cordis has hitherto received but little attention as an integral process; it has been treated under many and various partial names. Clinical observers generally confound it with myocarditis or with fatty degeneration; though

it agrees in strictness with neither. The affection is really anæmic necrosis. Fatty change and inflammation do in fact at times accompany it, but not as chief or primary conditions. Cardiac softening is altogether comparable with cerebral softening, or encephalomalacia. It is not a rare affection, and when at all extensive it brings about death by failure or rupture of the heart. It has been treated of by TAUTAIN (*De quelques lésions des artères coronaires comme cause d'altération du myocarde* Thèse de Paris 1878), and LAVERAN (*Union méd.* 23, 1878): compare also WILKS AND MOXON, *Path. Anat.* p. 122 London 1875; HUBER, *Virch. Arch.* vol. 89 and ZIEGLER, *ibid.* vol. 92; FAGGE, *Trans. Path. Soc.* XXV. (1874); TURNER, *Trans. intern. med. congress* vol. I. London 1881.

SAMUELSON (*Zeitschr. f. klin. Med.* II.), and COHNHEIM with v. SCHULTHESS RECHBERG (*Virch. Arch.* vol. 85) have recently investigated experimentally the effect on the heart of closing the coronary arteries. According to the latter clamping the coronary artery in the dog has no immediate effect on the heart's action, but after some 30 to 60 seconds the aortic blood-pressure sinks suddenly to zero, and the heart stands still in diastole. SAMUELSON operated on the rabbit and attempted to close and open the coronary artery alternately; he generally found that the aortic blood-pressure sank gradually. As in man the closure of the arteries must usually be gradual and at most affects only certain branches, the clinical symptoms usually differ somewhat from those which the experiments might suggest. The affection is manifested by gradually increasing failure of the heart's action, with angina pectoris and pulmonary congestion.

In cases of myomalacia we may sometimes see in the neighborhood of the softened fibres muscle-nuclei which are enormously enlarged, and stain very readily. ZIEGLER is unable to say what this may signify. In his researches on the subject he was never able to detect any sign of regeneration of muscle, so that there seems no reason to regard the appearance as evidence of any formative process. It is probably due to simple swelling or imbibition.

LANCEREAUX, IWANOWSKY, PUTJATIN (*Virch. Arch.* vol. 74), and USKOW (*ibid.* vol. 91) have pointed out that in various chronic affections of the heart certain changes take place in the cardiac ganglia; the changes may be degenerative or inflammatory.

CHAPTER IX.

HYPERTROPHY AND DILATATION OF THE HEART.

278. Enlargement of the heart, when not due to the presence of a tumor, is caused either by the dilatation of its cavities, or by the hyperplasia of its walls, generally of their muscular tissue but occasionally of their adipose tissue. Both dilatation and hypertrophy may exist at the same time.

In **simple dilatation** the auricular and ventricular cavities are enlarged, while the muscular walls are thinned by distention. The dilatation is often unilateral, that is to say confined to the right or to the left heart.

Hyperplasia of the cardiac tissues is generally due to true **hypertrophy of the muscular elements,** the walls becoming abnormally thick. It may be confined to the walls alone, or may extend to the trabeculæ and papillary muscles; indeed the latter may show the change more strikingly than the other parts. If no secondary degeneration has intervened the hypertrophied muscle appears firm and brownish-red in color. The general texture is not altered, but the muscle-elements are larger and more numerous than is normal. Higher degrees of hypertrophy are palpable even without section, the resistance and firmness of the walls being greatly increased.

The size of the cavities in hypertrophy varies much. If dilatation coexist with hypertrophy, so that the cavities are larger than normal, we speak of it as **excentric hypertrophy**; if they are smaller it is **concentric hypertrophy**; if they are of normal size, it is **simple hypertrophy.** Very frequently the hypertrophy is not general, but confined to one side only. Hypertrophy with dilatation of the right heart involves increase chiefly in the transverse dimensions; hypertrophy with dilatation of the left heart increases rather the longitudinal or apex-to-base measurement.

According to BENEKE (*Die anat. Grundlagen der Constitutions-anomalieen* Marburg 1878) the normal volume of the adult male heart is 260–310 ccm. for a stature of 167–175 cm.; or 150–190 ccm. for every 100 cm. of height. The growth of the heart is most rapid at two periods of life, namely during infancy, and at the time of puberty: it is much less rapid in the interval. In cases of hypertrophy the volume of the heart may rise to 500–700 ccm.; or 300–400 ccm. for every 100 cm. of height.

279. **Dilatation of the heart** is in part due to increased resistance opposed to the heart's contraction, and in part to textural change in its walls.

Hypertrophy of the heart is the result of increased work, and is a true functional hypertrophy. It of course implies not merely that increased work is called for, but that the conditions as regards increased nutrition of the cardiac tissues are sufficiently favorable; if the conditions were unfavorable the only result of increased strain (that is increased resistance to be overcome) would be dilatation.

The work required of the heart may be increased from various causes. Congenital narrowness of the aorta may induce hypertrophy of the left ventricle even in an infant, if it is well nourished. Other congenital affections leading to left hypertrophy are—affections of the valves producing incompetency or stenosis of the aortic orifice (Arts. 281–284); affections of the arteries, such as atheroma or sclerosis of the intima (Art. 297), and aneurysms (Art. 303), both of which increase the arterial resistances; partial destruction of the renal epithelium, and disorders of innervation, by which two latter causes the functional activity of the heart is increased. Pericardial adhesions may likewise induce compensatory hypertrophy. Right hypertrophy is the result of disease at the mitral or pulmonary valves, and of affections of the lungs in which the capillary area is seriously diminished or extensive pleural adhesions are formed.

Hypertrophy which follows as the result of visible anatomical lesions of the vascular system, or of the kidneys, or as the result of increased action due to nervous influences, is usually referred to as symptomatic hypertrophy. An idiopathic form of hypertrophy is also described, which is not referable to any increase in the heart's work; but this must be at least very rare. Even if in many instances we are unable to demonstrate anatomically the factors on which the hypertrophy depends, we cannot at once infer that during life no cause existed which involved an increased demand on the heart. Within recent years observation has shown that long-continued bodily exertion is particularly apt to cause functional hypertrophy; and according to Traube luxurious habits of life may produce a like result.

Fatty enlargement of the heart, obesity or lipomatosis, is due chiefly to the deposit of fat in the subpericardial connective tissue. The normal investment of fat is abnormally increased by increased supply and decreased consumption. The connective-tissue cells normally free from fat are transformed here and there into fat-cells, so that adipose tissue appears not only on the surface, but also in the intermuscular septa. In extreme lipomatosis the endocardium may also contain adipose tissue, and the function of the heart may be seriously interfered with.

The fact that hypertrophy of the left ventricle is associated with certain acute and chronic renal affections has been variously accounted for by various authorities. Some look for the cause of the hypertrophy in a general increase of the volume of the blood (TRAUBE, BAMBERGER), others in some change of its composition (BRIGHT, SENATOR, EWALD), others again in a wide-spread change (arterio-capillary fibrosis) in the walls of the smaller arteries (GULL and SUTTON). BUHL refers it to "post-inflammatory over-nutrition" of the heart. The outcome of recent research undoubtedly is—that cardiac hypertrophy following upon renal disease is dependent on increased arterial blood-pressure. COHNHEIM explains the increase of pressure thus: the degree of tonic contraction (*i. e.* the calibre) of the renal arterioles is determined simply by the proportion of urinary matters contained in the blood which circulates through them; the supply of blood to a diseased kidney is as great as to a healthy one; if abnormal resistances are interposed beyond the renal arterioles, in the capillaries or glomeruli, for example, the pressure in the renal arteries and so throughout the system must rise.

The most likely view is—that the increase of arterial pressure is due to increased resistances in the arterioles throughout the entire body When cardiac hypertrophy is induced by primary renal disease we must conclude that the resistances to the circulation outside the kidneys have been increased in consequence of the renal affection. The increased resistance is due to a contraction of the arterioles, and this is brought about either by the direct action of the urinary matters in the circulation, or by reflexes from the kidneys, or by stimulation of the vaso-motor centre.

References:—TRAUBE, *Gesamm. Abhand.* II., III.; JOHNSON, *Med. Chir. Trans.* XXXIII. (1850), LI. (1868); GULL and SUTTON, *ibid.* LV. (1872); BUHL, *Mitth. path. Inst. zu München*, 1878; BAMBERGER, *Samm. klin Vorträge* 173; EWALD, *Virch. Arch.* vol. 71; SENATOR, *ibid.* vol. 73; GRAWITZ and ISRAEL, *ibid.* vol. 77; ISRAEL, *ibid* vol. 86; COHNHEIM *Allg. Path.* II.; ROY, *Proc. Camb. Phil. Soc.* IV. (1881); ZANDER, *Morbus Brightii u. Herzhypertrophie* In. Diss. Königsberg 1881, and *Zeitschr. f. klin. Med.* IV. (with an elaborate discussion of the various theories); Discussion, *Trans. intern. med. congress* vol. I. London 1881.

CHAPTER X.

ENDOCARDITIS AND MYOCARDITIS.

280. **Acute endocarditis** is an inflammatory process set up by the presence in the blood of some irritant substance. It most commonly attacks the valves, but it may occur at any point of the endocardial lining. It usually takes the form of 'vegetative' or 'warty' endocarditis, which is characterized by the formation of small knotty and warty growths or vegetations, translucent or grayish or yellowish in tint, and projecting from the surface of the membrane. These are often overlaid and concealed by white or reddish or mottled thrombi.

The **valvular vegetations** generally form in rows along the lines of contact of the valves in closure; but they may be spread over the surface of the valves, or aggregated in groups to form large nodular or cauliflower-like excrescences. When they affect other parts, such as the wall of the auricle, the ventricular septum, the apex, etc., they are in general disposed irregularly, and may be aggregated into nodular masses or scattered in isolated patches. If the separate vegetations are all small but numerous and closely set, they may give the surface a granular or shaggy or merely turbid appearance; and close examination may be required to make out their individual existence. In the mildest forms no prominences above the surface are formed, so that the true nature of the patches is only to be made out with the microscope.

281. The vegetations consist essentially of subendocardial exudations and infiltrations.

The surface layers of the fully-developed vegetation (Fig. 125 *c*) are made up of granular (*e*) and fibrinous masses, which are for the most part merely coagulated exudations. Now and then patches appear which are distinguished by their fine and uniform granulation (*g*), and by their avidity for anilin-stains; they are possibly colonies of micrococci.

Among the granular masses certain peculiar colorless flakes or protoplasmic lumps (*f*) appear, which are probably nothing more than necrosed and coagulated endocardial cells. This is rendered more likely by the gradual transition observable between the persisting nucleated endocardial tissue and the non-nucleated lumps. The deeper layers (*d*) of the growth are infiltrated with small leucocytes, the infiltration extending in places to the superficial granular masses and to the deeper subendocardial tissues (*b*).

The genesis and the significance of the process are apparent from the consideration of such a vegetation. We see that it is an exudative inflammation, in which the exudation permeates the tissues and in part coagulates. Where coagulation takes place the tissue undergoes necrosis: where there has been only an infiltration of leucocytes the tissue persists.

The inflammatory process is therefore diphtheritic in its nature (Art. 103). It is closely related to superficial diphtheritic inflammation of the mucous membranes (Art. 435), and to pustulation of the cutaneous surface (Art. 388).

As we have already said, vegetations are not an invariable accompaniment of endocarditis. The inflammatory change is often recognizable only by the existence of more or less marked infiltration of the fibrous tissues of the lining membrane.

FIG. 125.—SECTION THROUGH AN ENDOCARDITIC VEGETATION.

(*From the auricle : hæmatoxylin staining :* × 150.)

a, endocardium.
b, subendocardial fibrous tissue, partly infiltrated with leucocytes.
c, the vegetation.
d, infiltrated leucocytes.
e, upper part of the growth consisting of fibrous and granular coagula.
f, colorless denucleated protoplasmic masses.
g, finely granular substance (? micrococci).
h, zone of transition from the undestroyed infiltrated tissue to the necrosed and coagulated tissue.

The cause of the inflammatory exudation is in some cases at least to be set down to the settlement of morbific organisms in the tissues. KLEBS (*Arch. f. exp. Path.* IX.) and EBERTH (*Virch. Arch.* vol. 72) have demonstrated the presence of microparasites in endocarditis. Whether the granular masses represented in Fig. 125 *g* are really micrococci is questionable, for the staining is not very intense. ZIEGLER met with a case of acute vegetative endocarditis, in which metastatic inflammations of the heart-substance and of the kidneys appeared, and in this he found colonies of micrococci in the blood-vessels of the affected organs. NAUWERCK recently found numbers of similar colonies in a case which

proved fatal after four months' duration. The colonies existed not merely in the thickened vegetations of the valves, but also in the still unaltered parts of the endocardium and in the muscular wall.

Endocarditis most commonly occurs associated with rheumatic affections, especially with acute general rheumatism, now regarded by some as of microparasitic origin. But it is also found in other conditions, as in measles and scarlatina and in fatal cases of nephritis, pneumonia, typhoid, septicæmia, etc. Very commonly, too, it develops in patients who are sinking under chronic suppurations, especially in the course of ulcerative cancer, or phthisis. LEYDEN says it also occurs after gonorrhœa. These facts point on the one hand to the conclusion that endocarditis is produced by bacteria, and on the other hand that the bacteria are not always of the same form, perhaps are of different species. In other words the etiology of endocarditis is probably multiform, not simple (Art. 204).

282. The ultimate course of endocarditis varies in different cases. The superficial granular masses and the investments of fibrin overlying the vegetations are incapable of organization. Small portions or patches may be absorbed, or may become calcified. Very often the growth softens and portions of it are swept off by the blood-current; and calcified masses may be swept off in like manner. In either case embolism is the result.

As necrosed masses are thus washed out excavations remain which are practically ulcers; they may be small or large. In so-called **ulcerative endocarditis** the destruction of tissue goes deeper still, so that a valve, for instance, may be deeply and extensively eroded by ulceration. In this way the weakened and infiltrated tissue which remains may give way under the pressure of the blood, and a sacculation, or acute valvular aneurysm, may be produced; or the process may go further and lead to perforation, and even to the detachment of a considerable fragment of the valve. Similar ulcerations may involve other parts, such as the *chordæ tendineæ,* which may in this way be severed from their valvular attachments.

Ulcerative endocarditis is usually the result of pyæmic or septic infection.

The vegetative and ulcerative forms pass gradually into each other, so far as their anatomical manifestations are concerned. The ulcerative form has usually been compared to the diphtheritic inflammations of the mucous membrane, but this is less than the truth; the vegetative form is likewise a diphtheritic inflammation with coagulative necrosis of the solid tissues. The two forms seem moreover to differ etiologically; the pernicious or ulcerative type being associated with septic or pyæmic processes, the vegetative with articular rheumatism. EBERTH (*Virch. Arch.* vol. 57 and *Corresp. f. schweiz. Aerzte* 1872) was the first who demonstrated the presence of bacteria in ulcerative endocarditis. Since then the fact has more than once been verified (MAIER, *Virch. Arch.* vol. 62; BURKART, *Berl. klin. Woch.* 1874; SANSOM *Lettsomian lectures* London 1883).

Perforation of the valves as a consequence of inflammation is not to be confounded with so-called **fenestration,** often found as a congenital anomaly in the sigmoid valves *above* the lines of contact in closure. This condition differs

essentially from the other, not merely in the difference of its site but in the absence of inflammatory infiltration or fibrous thickening around the hiatus.

283. **Results of endocardits.** If an attack of endocarditis does not prove fatal in its early or acute stage, certain plastic or formative inflammatory processes are set up at the affected spot, which result in the formation of new tissue and the cicatrization of the defect. The tissue in which the new formation starts is that which has not succumbed to the severity of the disease; the tissue in fact which is infiltrated but not necrosed. The raw material for new tissue is present, and the fixed cells of the old tissue are intact.

For weeks and months after the commencement of the disease the thickened tissues of the inflamed valves are still notably infiltrated with young cells, and may here and there have the appearance of ordinary granulations. Very probably the migrated leucocytes, and it may be the proliferous fixed cells, act as the builders of the new tissue; and their activity is maintained by the formation of new capillaries.

These plastic processes lead to more or less considerable thickenings of the endocardium. In the ventricles and auricles they appear as dense opaque white patches, which may be indefinite or sharply circumscribed.

The segments of the valves are thickened, hardened, coherent, and deformed in a multitude of ways. The tendinous cords are likewise thickened and shortened, and their ramifications abnormally adherent.

Degenerative change frequently attacks these inflammatory thickenings, and that in any of the forms mentioned in Art. 276. Fatty degeneration, and atheroma with calcification, are the commonest forms.

The result of these changes very often is that the valves are rendered functionally imperfect. Thickening and adhesion lead to narrowing of the ostia, or **stenosis**; retraction or deformity of the segments and cords to imperfect closure of the ostia, or **incompetence.** Both stenosis and incompetence may exist at the same orifice. It would be impossible to give in detail all the varieties that occur. In mild cases the thickening is slight and confined to the free margin of the valve and perhaps one or two of the cords. In severer cases the normal configuration of the valvular apparatus may be entirely lost. Thus the mitral opening is often reduced to a mere chink at the end of a funnel-like projection, surrounded by dense, firm, and all but immovable masses of fibrous tissue. If calcification ensue the parts round the ostium may become perfectly rigid and immovable.

We have already alluded to the results of valvular disease of this kind. In general terms they are these: the difficulties in the way of emptying the heart at each systole, whether from stenosis or regurgitation, are such that the blood tends to collect in the ventricle; the vascular system behind the diseased valve is permanently over-distended with blood, and so becomes dilated; and the heart hypertrophies to meet the

increased resistance, beginning with the part which serves to drive blood through the diseased valve.

284. **Myocarditis** not uncommonly accompanies endocarditis, the inflammation extending by continuity from the endocardium to the subendocardial and intermuscular connective tissue. In other cases the process may begin in the muscular tissue itself. In either instance the inflammation is characterized histologically by the appearance of an infiltration of leucocytes in the tissue of the heart-wall.

Two forms of myocarditis are distinguished, according as the disease results in induration or in abscess. **Indurative myocarditis** leads to hyperplasia of the intermuscular fibrous tissue, and the formation of ten-

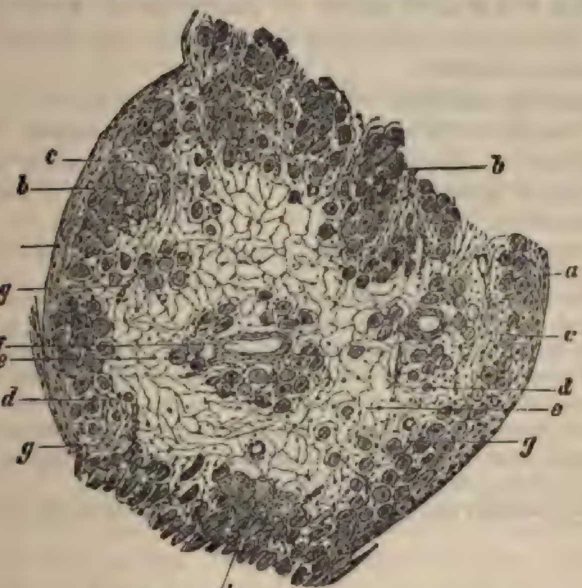


FIG. 126. SCLEROSIS RESULTING FROM MYOCARDITIS.

(Section through a fibroid trabecula: hæmatoxylin staining: × 40.)

a, endocardium.
b, normal muscle-cells.
c, hyperplastic connective tissue rich in cells.
d, atrophied muscle-cells amid hyperplastic connective tissue.
e, dense connective tissue with few nuclei and no muscle-cells.
f, vein, surrounded by a few intact muscle-cells.
g small blood-vessels.
h, infiltration of leucocytes.

don-like scleroses or thickenings (Art. 277), composed of glistening white bands or patches of dense fibrous tissue. As endocarditis is generally present at the same time, the endocardium will show similar tendinous streaks and patches on its surface. Not infrequently some of the muscular trabeculæ are transformed into coarse fibrous cords.

The new fibrous tissue (Fig. 126 *e*) when fully-developed is dense and almost free from cells; if the inflammatory process is kept up, it may still contain infiltrated leucocytes (*h*) in some spots.

The muscle-cells have in many places disappeared ; in other places, especially near the periphery, they remain but show evident signs of atrophy (*d*). When the inflammation is more recent, the tissue is grayer or more reddish, and richer in cells and in vessels. At first nothing is seen but an infiltration of small cells, amid which the muscle-cells appear in various stages of disintegration ; and sometimes hæmorrhage occurs. The disintegrated muscle-cells are not afterwards replaced.

The smaller scleroses have no serious effect on the heart's function ; but the larger ones which involve a considerable extent of the muscular substance may have a very harmful effect. The new tissue is not contractile, and so does not take a share in the general contraction of the heart ; while if it is at all pliable or distensible the blood-pressure may force it to give way and bulge into a sacculation, and thus an **aneurysm of the heart** is formed.

Purulent myocarditis usually accompanies pyæmic infections, and is due to bacteria which have reached the heart-muscle through the coronary arteries. Small yellowish or grayish abscesses are formed. They may break inwardly, and lead to cardiac ulcer ; or outwardly and set up pericarditis.

Larger myocarditic abscesses may lead to rupture of the heart.

As we have said, the ætiology of myocarditis corresponds in general with that of endocarditis ; but there are certain irritants which may set up myocarditis though they do not usually affect the endocardium. Thus according to LEYDEN (*Zeitschr. f. klin. Med.* IV.) the poison of diphtheria often causes myocarditis, while endocarditis a rare complication. ROSENBACH (*Virch. Arch.* vol. 79) found granular and waxy degeneration of the heart-muscle in diphtheria. LEYDEN moveover states that the virus of small-pox, of epidemic meningitis, or of relapsing fever, may bring about myocarditis.

On the myocarditis and sclerosis that follow myomalacia see Art. 277.

CHAPTER XI.

INFECTIVE GRANULOMATA, TUMORS, AND PARASITES OF THE HEART.

285. **Tubercle** is the commonest of the granulomata affecting the heart; **syphiloma** is more rare. In acute miliary tuberculosis the heart does not escape the general invasion; but it is much less common to find larger caseous nodules in its substance. When they do occur it is almost invariably in connection with like caseous nodules in the pericardium. Gummata are very rare. They lie in the wall of the heart embedded in dense hyperplastic fibrous tissue; and according to their age appear as soft reddish or grayish patches, or as dry yellow cheesy nodes. Simple inflammatory indurations of the heart-muscle occur as a consequence of congenital or acquired syphilis, and these are more common than gummata.

Of the **true tumors** several kinds may attack the heart primarily, such as sarcoma, fibroma, lipoma, myxoma, and myoma; but they are all of them rare.

Secondary tumors are more frequently found, especially secondary carcinomata. The tumor-germs, other than those that seize upon the heart from the pericardium, reach the heart-muscle through the circulation. The growths may be seated in the substance of the wall, or may protrude into the cavities, or into the pericardial sac. Occasionally tumors attack the heart by continuity from the mediastinum, the œsophagus, or the stomach.

The effect of such tumors on the heart will of course depend on their seat and size. If large they may interfere seriously with its action. Thrombi readily form on tumors which project into the cavities. Softening and ulceration of new growths may lead to rupture of the heart.

Of **parasites** *Cysticercus* and *Echinococcus* are found in the heart. *Echinococcus* (hydatids) may lead to its rupture.

For references see ORTH'S *Lehrb. d. spec. path. Anat.* vol. I. Berlin, 1883.

CHAPTER XII.

HYPOPLASIA AND DEGENERATION OF THE VESSELS.

286. A blood-vessel consists essentially of an endothelial tube; but all vessels above a certain size have their endothelial walls strengthened by the addition of connective tissue, elastic tissue, and muscle-cells; and all again above a somewhat larger size have nutrient vessels of their own, the so-called *vasa vasorum*.

The diseases of the vessels are processes affecting the vessel-walls alone, or the vessel-walls with the surrounding tissue; or they may form merely a part of some general affection of the parenchyma of the organs through which the vessels run. The latter is especially the case with the smaller vessels embedded in the substance of the organs.

The **malformations of the vessels** which have clinical importance have already been referred to in treating of the malformations of the heart. Here we need refer again only to the condition of general undergrowth or hypoplasia of the vessels associated with chlorosis, and characterized by abnormal narrowness of the channels and thinness of the walls, especially of the greater arteries. The very frequent anomalies of position, course, and distribution which are met with in arteries and veins are treated of in text-books of normal anatomy.

According to BENEKE (*Die anat. Grundlagen d. Constitutions-anomalieen* Marburg 1878) the circumference of the ascending aorta in a new-born infant is 20 mm., in an adult 60 mm.; the pulmonary artery measuring 23 mm. and 65 mm. in the two cases respectively. Above the bifurcation of the abdominal aorta the circumference in the adult measures 32 mm.

287. **Simple atrophy** of the walls of arteries and veins is observed in connection with general marasmus and atrophy of individual organs. After amputation of a limb the vascular trunks of the stump usually become smaller. Instead however of this simple and uncomplicated atrophy we more often find evidence of partial disappearance of some constituent (such as the muscular fibres) of the vessel-wall, the result of inflammatory or degenerative change.

Fatty degeneration of the vessels is the most frequent of all the degenerative changes to which they are subject. It usually attacks the inner and middle coats, more rarely the adventitia.

Fatty change of the intima is most commonly exemplified in the aorta,

but it is frequent enough in the larger arteries, including the pulmonary artery.

The slightest degree of fatty change is not apparent to the naked eye. More marked degrees are characterized by the opaque whitish or yellowish appearance of the affected spots, which are usually somewhat irregular in outline. The surface is at first smooth, but in latter stages it becomes uneven or velvety.

The process begins with the fatty degeneration of the cells, which become filled out with oil-globules (Fig. 127 *A*). If the change proceeds further the arrangement of the oil-globules ceases to be so definite as it is in the figure; they not merely occupy the place of the cells but also accumulate between the fibres of the intercellular ground-substance. In still more advanced cases subendothelial cavities are formed by softening. At this stage leucocytes generally appear, which have migrated from the

FIG. 127. *A*, CELLS FROM THE INTIMA OF THE AORTA SHOWING FATTY DEGENERATION.
(*Seen on the flat.*)
B, FATTY CAPILLARY FROM THE BRAIN.
(*Perosmic acid preparation:* × 800.)

vasa vasorum, and take up the fatty products of disintegration into their substance; it is in this way that fat-granule carrying cells arise.

The favorite seats of fatty change in the aorta are immediately above the valves, and at the places where the large and small arteries are given off. The change is most common in anæmic and in aged patients. In the pulmonary artery it seems most favored by causes producing stagnation in the pulmonary circulation, in consequence of which the carbonic acid of the blood is imperfectly removed from it. Spots of fatty degeneration occur in like manner in the lining membrane of the veins when the circulation through them is chronically impeded.

Fatty degeneration is common in the capillaries (Fig. 127 *B*), partly as the result of simple disorders of circulation, partly of changes in the blood itself such as are met with in infective diseases and in certain forms of poisoning (phosphorus or arsenic).

The tunica media may be affected as well as the intima, the fatty change specially attacking the muscle-cells, which in consequence often perish outright. The general course of the process is the same as in the

case of the intima; but its effect on the functions of the vessels is more serious. Thus degeneration of the middle coat may lead to rupture of the vessel; while calcification follows readily upon fatty change, and the vessel may thus lose its elasticity and contractility, and remain a mere rigid pipe.

The cells of the adventitia are found to become fatty in connection with like change either in the interior coats, or in the parenchyma of the surrounding organ; the change has no special significance. Not infrequently the fat found in the meshes of the adventitia is not produced there, but is merely deposited from the lymphatics.

See on this subject VIRCHOW (*Virch. Arch.* vols. 1 and 3, and *Gesamm. Abhand.* (1856) p. 493); LANGHANS (*Virch. Arch.* vol. 36).

288. **Amyloid degeneration** of the vessels is very frequently met with. As was pointed out in Art. 52 the vascular system is in a special way singled out as the seat of amyloid deposit. In the larger vessels the intima is most apt to be affected; in the smaller vessels the media, and to some extent the adventitia.

Hyaline degeneration (Art. 63) is the term used to describe certain morbid appearances in the vessel-wall, which have certainly not always the same significance. In the first place the term is applied to a peculiar transformation of the intima of the larger vessels, by which it is changed into a homogeneous connective tissue with few nuclei; in this atheroma often takes its rise (Art. 299). A second form of homogeneous change bearing the same name affects chiefly the smallest arterioles and capillaries; it is oftenest observed in the renal glomeruli, in the choroid, and in the brain. In the case of the capillaries the change is preceded by proliferation of the nuclei of the cells (OELLER); then homogeneous or hyaline deposits are formed on the exterior of the capillary tube, which are at first scattered but presently aggregate into masses encircling the tube. Thrombi are occasionally formed in the altered capillaries, and after a time they too assume a homogeneous appearance.

In the arterioles the change may extend to all the coats of the vessel, or be limited to one only; the change may here as in the capillaries be preceded by proliferation of nuclei; and thrombosis may likewise be set up.

The genesis of the hyaline deposit is not always easily determined. Some authorities hold that it depends mainly on the coagulation of extravasated red and white blood-cells. In other cases it is due to a homogeneous metaplasia of the connective tissue.

Calcification of the vessels occurs chiefly in cases where the nutrition of the vessel-wall is impaired, and where the tissue has already undergone some antecedent degenerative change. Thus calcification in the arteries is a very common sequel of fatty change; and also of sclerosis or atheroma (Arts. 297 and 298). The calcareous matter is deposited

in the intima or media. In the former it is mainly the sclerosed or atheromatous patches themselves which become calcified; so that definite and coherent calcareous plates are formed, which may be removed en-entire. In the case of the media the process may go so far as to convert the whole vessel into a hard and rigid tube; this occurs most commonly in the larger and middle-sized arteries of the trunk and limbs. The inner surface of such arteries has often a ribbed or corrugated appearance, fine white circular ridges running round the wall. If the intima be peeled off (and it is usually very loosely attached), it is seen that the ridges spring from the middle coat. The intima itself is sure to be more or less atheromatous.

The calcareous salts are deposited in small shining grains lying in the muscle-cells or in the intercellular tissue. In the middle coat of the aorta (Fig. 128) they lie irregularly in the spaces separating the elastic lamellæ.

Calcification of the capillaries is chiefly met with in tumors of the central nervous system.

FIG. 128. CALCIFICATION OF THE TUNICA MEDIA OF THE AORTA.
(*The deposit lies between the elastic lamellæ :* × 250.)

The veins may also be the seat of calcareous deposits, but much less frequently than the arteries. The deposits chiefly occur in dilated and varicose veins, and then generally in the inner strata of the middle coat.

Necrosis of the vessel-wall is generally a result of an inflammation set up in the surrounding tissue and resulting in general necrosis and disintegration. Diphtheria and caseous tuberculosis are of this kind; and the vessels undergo changes analogous to the changes in the other tissues affected. But besides this acute necrosis there is a more gradual 'necrobiosis' of the vessel-wall in which the tissue first becomes homogeneous and then breaks up; it mainly affects the intima (Arts. 297–299).

On hyaline degeneration of the vessels see Art. 63; THOMA (*Virch. Arch.* vol. 71); ZIEGLER (*Arch. f. klin. Med.* XXV.); LEYDEN (*Zeitschr. f. klin. Med.* II.); WEIGERT (*Virch. Arch.* vol. 79; JUNGE (*Arch. f. Ophthalm.* V.); SCHWEIGGER (*ibid.* VI.); OELLER (*Virch. Arch.* vol. 86); MEYER (*Arch. de physiol.* VII.).

CHAPTER XIII.

HYPERTROPHY AND HYPERPLASIA OF THE VESSELS.

289. True **hypertrophy of the arteries,** that is to say increase in all the coats of the walls without loss of structure, is seen in a marked form in the vessels which carry on collateral circulation after the occlusion of a larger artery. The increase is most remarkable when it depends on the occlusion of one of the large arterial trunks. The collateral vessels increase in length as well as in width and thus become convoluted, while the increase in the thickness of the wall is even greater in proportion. Local hypertrophy may likewise follow upon increase of blood-pressure, such as occurs in front of a contracted portion of the vessel. If the pressure of the blood be generally increased throughout the system, as it is in chronic Bright's disease, the smaller arteries may become universally hypertrophied.

The so-called anastomotic or racemose aneurysm (Art. 151) is mainly due to dilatation, convolution, and hypertrophy of arteries and capillaries. And in hypertrophy of the organs, as in ordinary development or in new-formations, the arteries tend to become more or less hypertrophied.

Veins and capillaries may hypertrophy like arteries, especially under the conditions just mentioned, which are associated with increased blood-supply.

Hypertrophy implies increase in the elements of the vessel-walls, but not in the number of the vessels; the latter is **hyperplasia,** and is an extremely common occurrence. In the General Pathological Anatomy we pointed out that the development of new-formations of any size involved of necessity the formation of new vessels; and in Art. 86 we described the mode in which this takes place. At first capillaries only appear; but by the multiplication of the elements of the walls and their progressive differentiation arteries and veins are ultimately elaborated.

CHAPTER XIV.

INFLAMMATIONS OF THE VESSELS.

290. We have already had occasion to allude to two varieties of inflammatory change affecting the walls of the vessels. From one point of view, we have spoken of an alteration in the vessel-wall as an essential factor in all inflammatory processes, this alteration being the condition antecedent to the quantitative and qualitative changes in the current of transudation from the smaller vessels into the tissues. The increased permeability of the vessel-wall permits the escape from the capillaries and veins, not only of liquid, but of large numbers of white and occasionally red blood-cells (Art. 96). The second form of inflammatory change dealt with was that concerned in the organization of thrombi (Art. 255). Here the vessel-wall became inflamed in consequence of the irritating presence of a foreign body, the thrombus itself; and the inflammation resulted in the development of granulation-tissue and a cicatrix within the vein or artery. In view of the ultimate result of the inflammation, we might describe it as a plastic obliterating endarteritis or endophlebitis.

But in addition to these two kinds of inflammatory vascular change we have a series of others which have their seat in the substance of the vessel-wall and lead to temporary or permanent changes extending to a part or the whole of its thickness. **Arteritis** and **phlebitis** are used to describe these parenchymatous inflammations of the vessel-wall. They may arise as primarily vascular affections and be confined to the proper tissues of the vessels; or the surrounding tissues may be likewise involved; or the vascular affection may be secondary to an existing inflammation of the surrounding tissues. The latter occurs in the case of minute vessels embedded in the tissues, and is to be clearly made out only by the aid of the microscope.

291. **Purulent arteritis,** issuing in suppuration and destruction of the wall of the artery, is generally a secondary process occurring within suppurating wounds and ulcers. Inflammation and necrosis extend by continuity from the surrounding tissues to the vessel, destroying first the adventitia and then the other coats. The wall appears thickened and yellowish or grayish in color; the intima is turbid, yellowish or grayish, and infiltrated with pus. Often the brittle or rotten vessel gives way, and hæmorrhage follows. Secondary hæmorrhage in wounds, hæmopty-

sis from phthisical lungs, hæmorrhage from cancerous ulcerations, etc., are all of this nature; and in the same way fatal bleeding may occur from suppurative inflammation of the umbilical cord in infants. At times, as in tuberculosis, the necrotic process takes on a caseous character. Suppuration in wounds is chiefly conditioned by the invasion of micrococci.

Sometimes purulent arteritis with necrosis is due to the entrance of irritant matters into the blood, as happens in embolism where the emboli are virulent or infective (Art. 116). When the destructive proces spreads from the vessel to the neighboring tissue, abscesses are formed.

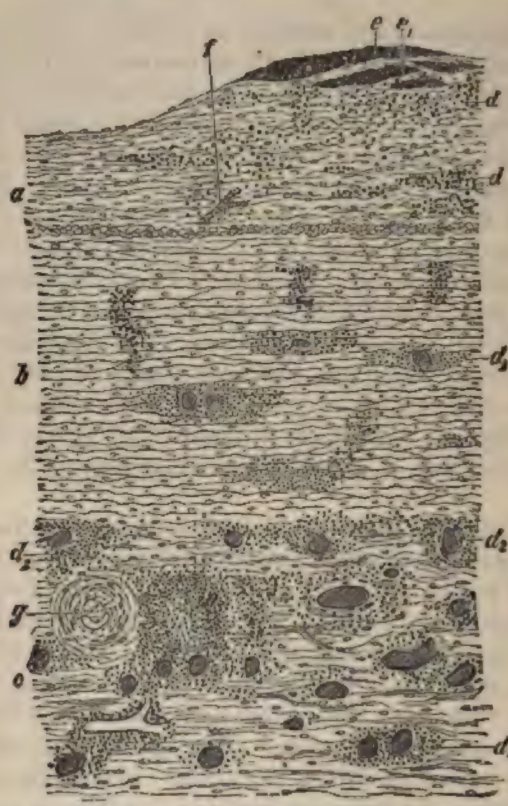


FIG. 118.—SECTION OF THE AORTA IN ACUTE AORTITIS.
(*Carmine staining* : × 45.)

a, intima thickened by previous inflammation.
b, media with infiltrated leucocytes d_1.
c, adventitia with infiltrated leucocytes d_2.
d, infiltrated leucocytes.
e, granular fibrin lying on the intima.
e_1, the same within the intima.
f, blood-vessel within the hyperplastic intima.
g, small artery contracted by sclerosis of its walls.

The pus-corpuscles which in these processes accumulate in the substance of the vessel-wall are in part derived from the vasa vasorum, in part from the surrounding vessels.

Purulent phlebitis occurs under the same conditions as purulent arteritis. The walls of the veins are thickened and discolored, and the intima is turbid. The lumen very frequently contains fresh or softened and puriform thrombi. The purulent inflammation of the vessel may be preceded or followed by coagulation of its contents. The relation of the two processes is often as follows: incipient inflammatory change in the vessel-wall gives the condition for thrombosis; a thrombus forms and is invaded by micrococci; it then breaks down into a puriform irritant mass, which in its turn intensifies the inflammatory change in the vessel-wall to the pitch of suppuration and necrosis. Examples of the process (known as **thrombophlebitis**) are frequently met with, as in the radicles of the portal vein, near ulcerated patches in the intestine, such as occur in dysentery and in the veins of suppurating wounds. If the softened and infected thrombi pass into the general circulation, we have pyæmia and metastatic abscesses as the result.

292. **Hyperplastic arteritis**, in its early stages, is best studied in cases of what is called **acute aortitis,** an affection which however is rarely seen exemplified in the post-mortem room. It is rapidly fatal only when it is very extensive; minor cases usually recover.

The changes it produces are exactly similar to those described under endocarditis and myocarditis.

The inner lining of the affected vessel looks turbid and somewhat loosened, or gray translucent granulations rise from its surface, or larger irregular vegetations resembling closely those seen in the endocardium. Thin films of fibrin often lie over the inflamed patches.

The middle coat and the adventitia, but especially the latter, show patches of gray or grayish-red; but it rarely happens that their extent is large enough to allow them to be readily recognized by the eye alone.

When the more seriously affected parts are examined microscopically, it is seen that all the coats of the artery are attacked; the characters of the change being the extreme distention or congestion of the vasa vasorum, and the presence of cellular, coagulated, and granular masses of exudation (Fig. 129 d d_1 d_2 e e_1). Sometimes the adventitia (c) shows the most striking changes, being greatly thickened in consequence of abundant cellular infiltration and of nodular clusters of cells (d_2) surrounding the vasa vasorum. The infiltrations in the media are also clustered around the vasa vasorum (d_1), and often reach considerable size.

The intima contains accumulations of leucocytes (d) in the meshes of its connective tissue, in addition to granular fibrinous coagula (e e_1) which lie either within (e_1) the distended meshes or on the surface (e).

The cellular infiltration in aortitis is derived from the vasa vasorum, as is evidenced by the clustering of the cells around these vessels. Where the cells are more remote from the vessels, as in some parts of the intima, we conclude that they have migrated.

References :—KÖSTER, *Sitzungsber. d. niederrhein. Gesell. f. Natur u. Heilk. in Bonn* 1877 ; KÖSTER, *Die Pathogenese d. Endarteritis* 1871 ; JACCOUD, *Path. interne* I. 1873 ; STROGANOW, *Recherches sur l'origine des eléments cellulaires dans l'endartérite de l'aorte, Arch. de physiol. norm. et path.* 1876 ; WINIWARTER, *Arch. f. klin. Chir.* XXIII. ; LÉGER, *Étude sur l'aortite aiguë* 1878 ; JAHN, *Virch. Arch.* vol. 72 ; TROMPETTER, *Ueb. Endarteritis* In. Diss. Bonn 1876 ; TALMA, *Virch. Arch.* vol. 77 ; GIOVANNI, *Arch. ital. d. biol.* I. ; CORNIL and RANVIER; *Man. of Path. Hist.* I., 1882, *Arch. de physiol.* 1868 ; POULIN, *Gaz. hebdom.* 1879 ; ISRAEL, *Virch. Arch.* vol. 86 ; ORTH, *Lehrb. d. spec. path. Anat.* I., 1883.

293. If the patient does not die during the early stages of the disease, the process of repair begins and new fibrous tissue and capillaries are developed at the affected spots. When the exudation has been slight it may be entirely re-absorbed ; but if the inflammation is kept up fibroblasts are developed, and from them new fibrous tissue. Whether the fixed tissue-cells or the white blood-cells take the chief share in building up the new-formed tissue is hard to determine.

Three forms of arterial inflammation are distinguished according to the coats chiefly affected, namely endarteritis, mesarteritis, and periarteritis ; but the forms very frequently occur in combination.

If **endarteritis** becomes chronic, and new fibrous tissue is formed in the intima, broad slightly raised *plaques* are produced, which often appear in large numbers and of great size in the larger arterial trunks, and especially in the aorta. As Fig. 129 (*a*) shows, they consist of dense fibrous tissue resembling scar-tissue ; the normal structure of the intima is usually lost. New vessels are nearly always formed (Fig. 129 *f*). In other cases the new tissue is looser, more resembling areolar or mucoid tissue. Such hyperplasias of the intima are called **scleroses** (Arts. 297–298) ; they occur both in large and in small vessels, and in the latter may produce considerable contraction of their calibre. The process has therefore been also described as **obliterating endarteritis.** Once it has begun it is apt to recur, increasing the size of the old patches and starting new ones ; it is thus progressive in its character.

Mesarteritis is generally an accompaniment of endarteritis. Fibrous deposits appear in the middle coat, while the normal elements and especially the muscular fibres perish by degrees. The changes in the middle coat seldom reach the same pitch as those in the intima ; but here and there the normal tissue may be entirely displaced by new scar-tissue.

Periarteritis leads to fibrous thickening and condensation of the adventitia. In vessels which lie freely in the tissues the thickenings are diffuse or aggregrated into coarse bands or nodes. The latter variety has been described by KUSSMAUL and MAIER as *periarteritis nodosa.*

Hyperplastic phlebitis corresponds to hyperplastic arteritis, and like it is an inflammation leading to fibrous hyperplasia. The forms endophlebitis, mesophlebitis, and periphlebitis are distinguishable. It is rarer than arteritis as a simple or primarily vascular disorder. The thickenings formed in the intima of the veins are by no means so remark-

able as those of the arteries. Fibrous hyperplasia of the walls of the veins most frequently results from venous thrombosis, or from chronic parenchymatous inflammations of the surrounding tissues which have spread to the veins.

KUSSMAUL and MAIER (*Deutsch. Arch. f. klin. Med.* I.) met with a case in which the arteries of the most diverse organs were beset with nodes and nodules from the size of a pea to that of a millet-seed. The nodules were partly cellular and partly fibrous; they were seated chiefly in the adventitia, but some of them were in the media. MEYER describes a like case (*Virch. Arch.* vol. 74).

294. The **ætiology of the hyperplastic inflammations** of the vessel-wall is not always the same. It is to be remembered that the inflammatory processes which lead to fibrous hyperplasia in any organ may all of them affect the included vessels, and may thus lead to thickening of the vessel-walls. Often the adventitia is the coat most affected, but the other coats do not by any means always escape. These forms of arteritis and phlebitis are obviously due to the same causes as those which lead to the corresponding organic affections.

Even the inflammations which are limited to the vessels themselves are not always due to the same kind of irritant or injury. The case resembles that of endocarditis, an affection which as we have seen may spring from more than one source. In the first place, the irritants or injuries which produce endocarditis may also produce endarteritis; the evidence of this being that in many cases both affections occur simultaneously. But it would seem that there are more varieties of injury capable of producing arteritis than of producing endocarditis; or at least that vascular inflammations occur under conditions where it is unusual to find endocarditis. Of the causes which may set up chronic vascular inflammations the chief are syphilis and tuberculosis.

295. **Syphilitic arteritis** was first closely studied by HEUBNER, who showed that it is of frequent occurrence. It is found in two chief forms, that is to say either as an independent disorder, or as part of a local syphilitic affection. In the former the affected vessel shows white or grayish thickening of the intima and of the adventitia. The vessel, such as a cerebral artery, may thus be beset with circumscribed grayish translucent patches, or be transformed into a coarse white or grayish cord. This form is not to be distinguished, either with the eye or the microscope, from arterial thickening due to non-syphilitic fibrous hyperplasia. The second form of syphilitic arteritis occurs in the midst of foci of syphilitic disease affecting the tissues generally; the vessels are surrounded either with diffuse cellular infiltrations (the so-called gummatous granulations), or with dense cicatricial tissue (Arts. 128–130). In such cases the coats of the vessel are more or less altered and thickened (Fig. 130).

The intima (*a*) and the adventitia (*d*) are usually more thickened than the media (*c*). While the process is still recent, not having yet passed the stage of granulation, the thickening of the intima is partly

due to an abundant development of fibrocellular tissue (*e*). The cells are in part small and round, in part fusiform or stellate (*f*) corresponding to certain forms of fibroblasts. The adventitia is similarly altered. The media is usually but little beset with migratory cells.

In more advanced cases where fibroid change has succeeded active inflammation, the thickened coats of the vessels are more fibrous and less rich in cells. The middle coat is either little altered, or here and there atrophied and fibrous. There is nothing specific in the histological character of the process; all we can say is that in the ordinary non-syphilitic inflammations of small arteries it is unusual to have so abundant an infiltration of cells as in syphilitic inflammations, and that the adventitia especially is not so subject to marked alteration.

The thickening of the vessel-wall in syphilis is often very considerable; it may indeed become so extreme that the lumen of the affected artery may be almost or entirely occluded.

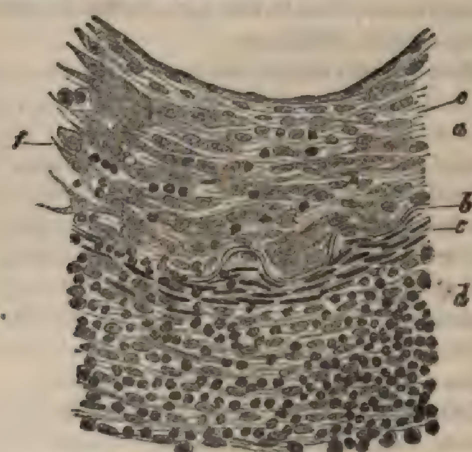


FIG. 130. SYPHILITIC ARTERITIS.

(*Carmine staining*: × 150.)

a, greatly thickened intima, the thickening due to fibrocellular tissue (*e*) and new-formed cells (*f*).
b, fenestrated elastic membrane, broken through on the left side.
c, muscle-fibres of the media, beset on the left with large and small leucocytes.
d, adventitia thickened by fibrous hyperplasia and cell-infiltration.
e, fibro-cellular tissue of the intima.
f, new-formed cellular tissue with infiltrated leucocytes.

The walls of the veins are likewise subject to gummatous syphilitic inflammations.

The diagnosis of syphilitic arteritis rests in general more on the naked-eye appearances than on the minute histological characters. The specific nature of the affection will be determined mainly by the presence of other localized syphilitic affections, especially of a gummatous kind. If these last are not found, we must not pronounce the disease to be syphilitic unless we can find sure signs of it elsewhere, or unless we have excluded all other possible causes for the vascular

changes. There are no certain histological criteria for deciding on the presence of syphilis (HEUBNER, *Die luetische Erkrankung der Gehirnarterien* Leipzig 1874; *Ziemssen's Cyclop.* XII.). Even the abundance of cells found in the adventitia is not pathognomonic, for in the cerebral vessels especially tuberculosis may give rise to exactly similar appearances. See BRISTOWE (*Trans. Path. Soc.* 1859); HUGHLINGS JACKSON (*London Hosp. Reports* 1868); BAUMGARTEN (*Virch. Arch.* vol. 73, 76, 86, the last contains a number of references); VON LANGENBECK *Arch. f. klin. Chir.* XXVI.); FRIEDLÄNDER (*Cent. f. d. med. Wiss.* 1876); EHRLICH (*Zeitschr. f. klin. Med.* I.); HUBER (*Virch. Arch.* vol. 79); BIRCH-HIRSCHFELD (*Arch. d. Heilk.* XVI.); LANCEREAUX (*Gaz. d. Hôp.* 21, 1876); GREENFIELD, GOWERS, and others (*Trans. Path. Soc.* 1877-78).

296. **Tuberculous inflammation of the vessel-walls** is very common, inasmuch as arteries and veins running through tuberculous organs are readily invaded by the disease. Tubercles and more diffuse tuberculous patches may appear in their walls; and if the granulomatous focus becomes caseous, the vessels undergo the same transformation. If the diseased vessel be an artery it often ruptures and gives rise to hæmorrhage; if it be a vein the disintegration of the wall may admit products of disintegration and bacilli into the blood-current. The result is an eruption of tubercles at the spot whither the bacilli are carried by the blood.

Fibrous hyperplasia may also be set up as a consequence of tuberculous inflammation. Most commonly it is the adventitia which becomes thickened, though at times a like thickening is met with in the intima. It may become so considerable that the vessel is almost or quite occluded. The same result may follow when thrombosis is set up in a vessel whose wall is beset with tuberculous granulations.

References:—RINDFLEISCH, *Ziemssen's Cyclop.* V.; MARTIN, *Recherches anat.-path.* Paris 1879; CORNIL, *Journ. de l'anat.* XVI.; KIENER, *Arch. de physiol.* VII.; MÜGGE, *Virch. Arch.* vol. 76; ARNOLD, *ibid.* vol. 88; WEIGERT, *ibid.* vols. 77, 88.

CHAPTER XV.

SCLEROSIS AND ATHEROMA.

297. **Sclerosis** in an artery implies the existence of local thickenings of its inner coat. They appear as slight broadened prominences, rising above the level of the normal intima as definite flat or convex *plaques* or patches. The margins may be steep or sloping, the surface is smooth. The patches may be translucent or almost gelatinous, or cartilaginous, or white and densely fibrous.

These patches appear in arteries of all sizes—from the aorta just above its valves to the smallest arteriole. They are often few in number; but in other cases they are extraordinarily numerous, cases occurring in which the intima of the aorta is so beset that there scarcely remains a healthy spot on its surface.

If the sclerosis is at all marked there are always found, in addition to the grayish or cartilaginous patches, other *plaques* of an opaque white or yellowish-white color. These may be smooth or rough; and not infrequently the tissue has disintegrated and fallen away from them, leaving so-called ulcers with white detritus lying on their floors; or the rough and ulcerated spots may be covered with thrombi. The white or yellowish *plaques* are known as **atheromatous patches,** and the eroded spots as **atheromatous ulcers,** the process as a whole being described as atheroma of the arteries. It is thus a sequel of sclerosis.

Very often a third change is associated with these, namely the **calcification** of the affected spots. When this occurs the white atheromatous patches become hard and rigid to the feel, giving one the impression of a plate of bone lying beneath the superficial layer.

In the veins these changes are much less common, and in general much less marked; but they do sometimes occur. Calcification is oftener met with than simple atheroma.

References:—WILKS and MOXON, *Path. anat.* London 1875; MEYER, *Arch. d. physiol.* VII.; NEUMANN, *Arch. f. mikrosk. Anat.* XVIII.

298. Sections show well the seat and characters of sclerotic and atheromatous change (Fig. 131). The intima (*a*) is generally the most affected, while the media (*c*) is often unaltered, and the adventitia (*h*) only slightly infiltrated. In other cases the adventitia may be somewhat thickened and the media atrophied. The change in the intima consists of more or less extensive but generally unilateral thickening. At the

oints where the altered passes into the unaltered tissue the thickening is made up of fibrous tissue (g) more or less notably infiltrated with leucocytes. The same is true of the innermost layers of the altered intima; but the deeper layers in contact with the elastic bounding membrane consist of pale indistinctly fibrillated tissue (e), which is devoid of nuclei and almost entirely necrosed; they contain numerous aggregations of granular detritus (f). The granular masses consist partly of albumen, partly of fat, and older foci of softening nearly always contain tablets of cholesterin (f_1). Atheroma thus appears to be essentially a necrosis with granular and fatty disintegration of the thickened intima.

The atheromatous ulcer is produced by the advance of the disintegrating process towards the lumen of the vessel, and rupture of the innermost layers of the intima. We may conceive how readily such a

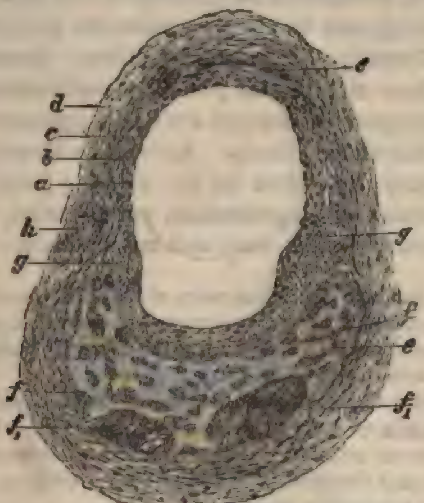


FIG. 131. ATHEROMATOUS CEREBRAL ARTERY (× 50).

a, intima considerably thickened.
b, bounding elastic lamella of intima.
c, media.
d, adventitia.
e, necrosed denucleated tissue with masses of fatty detritus f and
f_1, detritus with cholesterin-tablets.
g, infiltrated leucocytes in the intima.
h, infiltrated leucocytes in the adventitia.

rupture might occur, if we note that on the post-mortem table very slight pressure on an atheromatous patch often suffices to break in the surface layer and convert the patch into a cavity.

299. As regards the **genesis of sclerosis and atheroma** we must remember (Art. 292–293) that thickening of the intima may be the result of a process beginning with inflammatory infiltration, and leading to the formation of new fibrous tissue. We may therefore say that sclerosis and atheroma of the arteries are in many cases the result of a chronic endarteritis, which began as an acute affection.

But this is not always so; or at least we have not always evidence enough to justify the hypothesis. Especially is this the case with the gradually developed forms found in advanced age. The affection is either limited to the aorta or to the arteries of one or other organ, or it is more or less diffused over the entire arterial system. This **senile atheroma** does not begin in inflammation, but either in degeneration or metaplasia.

VIRCHOW has shown that in many instances the first step is a kind of gelatinous degeneration of the intima, leading to swelling and loosening of its texture. Then ensues proliferation of the tissue-elements of the intima, which may produce new fibrous tissue and bring about a thickening of the inner coat. But in extreme old age it is commoner to find the intima undergoing a kind of homogeneous or hyaline change, which is associated with a permanent thickening of its substance. Here and there the thickening may become considerable (Art. 288), and lead to the formation of raised *plaques* and patches. Retrogressive changes follow close on these metaplastic processes, and inflammation at length appears. The retrogressive changes are fatty degeneration, necrosis, and disintegration of the altered tissue. As we have already said, such retrogressive changes may themselves be the starting-point of the affection. When once the process of degeneration, proliferation, and inflammation is started, it generally spreads more and more widely.

We are not as yet able to define more closely the precise limits of the processes leading to atheroma, namely primary inflammation, primary metaplasia, and primary degeneration. In many cases we can only form hypotheses as to the mode in which atheroma has arisen.

The process leading to sclerosis and atheroma in the aged is often alluded to as **arteritis deformans,** or *malum senile arteriarum.* It has been compared with the affections known as arthritis deformans and *malum senile coxæ* (VIRCHOW, *Virch. Arch.* vol. 4, and *Gesamm. Abhandl.* (1856) p. 496); and the processes have indeed much that is apparently analogous.

LANGHANS (*Virch. Arch.* vol. 36) and KÖSTER (*Virch. Jahresb.* 1875) assert that a certain amount of thickening of the intima is so common in old age, that it may be regarded as physiological. GIOVANNI (*Arch. ital. de biol.* I.) maintains that disorders of the innervation of the vessels may lead to atheroma; compare LEWASCHEW (*Virch. Arch.* vol. 92). ISRAEL (*Virch. Arch.* vol. 86) observed endarteritis in rabbits, in which he had experimentally caused one kidney to become contracted.

300. Sclerosis and atheroma often give rise to serious **disturbance of the circulation** and with it of the nutrition of the parts supplied by the affected vessels. Apart from the resistances to the blood introduced by the deformation of the inner surfaces of the blood-channels and the loss of elasticity of their walls, there is occasionally a considerable narrowing of the calibre (Fig. 131), and this may become so great that the artery is at length completely occluded (as in obliterating endarteritis). As the various prominences encroaching upon the lumen meet and coa-

lesce the vessel may ultimately be transformed into a solid cord. If collateral circulation is not speedily set up, the blood-supply of the part is cut off, and anæmic necrosis ensues. This is a very common occurrence in the brain. It may take place not only in small arteries but even in the largest trunks, especially at the points where branches are given off. Thus, for example, the subclavians and carotids may be occluded by thickening of the intima at their points of origin from the aorta.

A second result is thrombosis. It is produced by the change in the vessel-wall on one hand, and by the slowing of the blood-stream on the other. Minor vessels which are already narrowed may be completely blocked up by intercurrent thrombosis. In the aorta parietal thrombi are common. If they are loosened and swept off they cause embolism; and the same result follows when particles are carried away from atheromatous ulcers. Atheroma of the arteries may likewise lead to morbid dilatation (Art. 301) of the vessel, or even to rupture. Both results are due to the textural changes, and the diminished power of resisting the blood-pressure which the changes involve.

CHAPTER XVI.

CHANGES IN THE CALIBRE OF THE VESSELS.

301. A **true aneurysm** is a localized dilatation of an artery involving all three of its coats. When the dilatation has persisted for a time one or other of the coats may atrophy; the media being the first to disappear, while the intima often follows. In this way the wall of the aneurysm may ultimately in places consist of the adventitia alone.

When the dilatation extends over a considerable section of the artery, when for instance the entire thoracic aorta is uniformly dilated while retaining its cylindrical form, we have a **diffuse** or cylindrical aneurysm; a spindle-shaped dilatation constitutes a **fusiform** aneurysm; a localized unilateral bulging is a **sacculated** aneurysm; while an artery with some of its branches which is dilated and convoluted, and it may be in parts sacculated, is described as a **cirsoid** aneurysm (or less aptly an aneurysmal varix, which term has properly another signification, Art. 311).

The forms just mentioned may of course be combined in various ways, so that intermediate and transitional varieties are common. In the case of sacculated aneurysms the diameter of the opening into the sac is often less than that of the sac itself.

The **racemose or anastomotic** aneurysm (otherwise described as an arterial vascular tumor) is a distinct variety. Here, as has been mentioned in Arts. 151 and 289, we have to do with a general dilatation of a multitude of arterial twigs and capillaries accompanied by hypertrophy of their walls.

Abnormal width of the arteries generally, apart from localized or aneurysmal change, may occur as a congenital or at least developmental anomaly.

302. The **development of an aneurysm** is in general to be referred to some pre-existent disease of the arterial coats. Sacculations are especially apt to occur when the intima and media are simultaneously affected by active disease or degeneration. Sclerosis and atheroma are the commonest causes, especially when the media also undergoes degeneration. In other cases affections of the adventitia may lead to aneurysm, when they are such as extend also to the media and set up inflammation or muscular degeneration there. All these affections diminish the elasticity and strength of the arterial wall, so that it stretches and gives way before the pressure of the blood. In accordance with the common mode

of genesis, we find the intima in most aneurysms highly atheromatous; the muscular elements of the middle coat are fatty and disintegrated or lost altogether; and the elastic fibres show signs of granular change. The media or intima or both may here and there be wanting entirely; while the adventitia is usually thickened and infiltrated with inflammatory exudations.

A form of aneurysm whose genesis is different has been described by PONFICK (*Virch. Arch.* vol. 58) under the title of the **embolic** aneurism. Fragments of calcified endocarditic vegetations lodge as embolisms in the wall of an artery, it may be in the brain for example; there they bore or work their way into the tissue of the wall, until at length it gives way and a sacculation is formed. Another special form is the so-called **hernial** aneurism, produced by the hernial protrusion of the inner coats through a weak or eroded place in the outer coat or sheath.

CHARCOT (*Senile and chronic diseases* (New Syd. Soc.) 1881) thinks that aneurysms start in degeneration not of the intima but of the adventitia, the inflammatory thickening of which induces atrophy of the muscular coat. ZIEGLER'S observations lead him to believe that this mode of development (from periarteritis followed by muscular atrophy in the media) does occur; but in the arteries of the brain, on which CHARCOT specially bases his conclusions, the process generally starts with the intima. The accumulations of infiltrated cells seen in the adventitia in such cases are secondary (VIRCHOW, *Virch. Arch.* vol. 3; CHARCOT and BOUCHARD, *Arch. de physiol.* 1868; LIOUVILLE, *Anévrysmes miliaires* Thèse de Paris, 1871; ROTH, *Corresp. f. schweiz. Aerzte,* 1874; KRAFFT, *Die Entstehung der wahren Aneurysmen* In. Diss. Berne 1877).

For references to aneurysm depending on embolism see CHURCH (*St. Barth. Hosp. Reports* 1870), GOODHART and others (*Trans. Path. Soc.* 1877).

303. **Seats of aneurysm.** Aneurysms most commonly occur in the thoracic aorta; they may be diffuse, fusiform, or sacculated. Their favorite seat is the ascending and transverse parts of the arch. They often reach an astonishing size, and press against the sternum and costal cartilages, or against the lungs and the spinal column, according to their position. Soft or yielding parts are pushed aside or compressed, rigid parts like the bones of the sternum or spine are eroded or absorbed. The costal cartilages and intervertebral discs resist the pressure better, so that while the vertebral bodies are often deeply excavated the discs persist almost unchanged. The tissue immediately surrounding an aneurysm is in some parts infiltrated with inflammatory products, in others thickened and fibroid. It is the inflammation set up around the aneurysm which leads to the absorption of the bone it presses upon.

The abdominal aorta is likewise a common seat of aneurysms, which may reach a very considerable size.

The popliteal artery is the vessel most subject to aneurysm after the aorta; and then follow the other trunks, namely the carotid, subclavian, innominate, axillary, iliac, splenic, hepatic, renal, hypogastric, etc. The sacs formed in these arteries are very seldom of anything approaching the

size of aortic aneurysms. True cirsoid aneurysms affect chiefly the common iliac and its branches, anastomotic aneurysms chiefly the vessels of the head. Somewhat indefinite dilatations are occasionally met with in the trunk of the pulmonary artery, but they are scarcely to be described as aneurysmal; in rare cases the valvular sinuses are more or less abnormally bulged. Large aneurysms of the pulmonary artery are very rare.

Aneurysms of the smaller arteries of the brain are of considerable importance. Aneurysmal sacculations of the arteries of the base may reach the size of a pea or of a bean. In the smaller arteries they are naturally smaller, and often cannot be made out with a lens (**miliary aneurysms** of CHARCOT). General or diffuse dilatation is met with chiefly in the basilar artery.

The small aneurysms met with in the twigs of the pulmonary artery in phthisis have a special interest. They are formed in consequence of inflammatory destruction of the vessel-wall starting in the adventitia, and belong in part to the class of hernial aneurysms.

304. **Consequences of aneurysm.** An artery which has once become aneurysmally dilated never returns to its normal state; the dilatation rather tends steadily to increase. The walls at the same time become thinner, inasmuch as the inflammation set up is unable to furnish any efficient substitute for the loss of healthy tissue. The consequence is that the sac ultimately gives way at some point or other, and, especially in the case of aortic aneurysms, **fatal hæmorrhage** ensues. Dangerous hæmorrhage may follow the rupture of arteries that are by no means large, notably those of the brain; fatal cerebral hæmorrhage or **apoplexy** is a very common occurrence. So too the rupture of minute aneurysms in the lungs often leads to fatal **hæmoptysis** in phthisis.

It is only in comparatively small arteries that the aneurysm is completely obliterated by the filling up of the sac with cicatricial tissue; probably the formation of such tissue is always preceded by the deposit of thrombi in the sac. The thrombi are then replaced by fibrous tissue in the manner described in Arts. 255 and 256. In large aneurysms we frequently find massive firm laminated decolorized or mottled **thrombi** more or less completely occupying the cavity. At various points we may find evidence of partial proliferation of the elements of the inner coat in contact with the thrombi, leading to the development of fibrous tissue; but the thrombi never undergo complete organization.

These somewhat incoherent thrombi form but an imperfect defence against the danger of rupture, as the blood may work its way between the thrombus and the vessel-wall; while the thrombi themselves may undergo softening, disintegration, or even liquefaction: occasionally calcareous salts are deposited and they become calcified.

CHARCOT asserts (*Senile and chronic diseases* 1881) that cerebral hæmorrhage always depends on the rupture of an aneurysm more or less minute. EICHLER

(*Deutsch. Arch. f. klin. Med.* XXII.), ZENKER (*Naturforscherversamm.* 1872), and ROTH (*Corresp. f. schweiz. Aerzte* 1874) admit that aneurysms are very generally found in such cases. But they are occasionally absent, and the truth probably is that they are a frequent but not an invariable cause of apoplectic hæmorrhage. See QUINCKE (*Ziemssen's Cyclopædia* VI.); LANCEREAUX (*Traité de Path.* II.).

305. Dilatation of the capillaries is usually referred to as **capillary ectasis** when it is general; more localized dilatations are called **capillary aneurysms.** Ectasis chiefly occurs as a result of chronic disorders of the circulation which lead to over-distention of the capillaries with blood; in other words as a result of long-standing congestion or engorgement. The pulmonary capillaries and the intralobular hepatic vessels in mitral disease afford good examples. The condition often affects the capillaries over a wide area.

FIG. 132. DILATED OR ECTATIC CAPILLARIES.
(*From an angioma or telangiectatic glioma of the brain:* × 200.)

Capillary dilatations limited to particular spots are usually due to causes a different kind. Some are congenital, as in so-called vascular nævi. These have already been treated under the head of angiomata in Art. 149.

Fig. 132 gives an idea of their general disposition. Congenital dilatations of the capillaries are most usually met with in the skin; but they may occur elsewhere, as for instance in the brain (cerebral nævus).

Acquired capillary ectases generally arise in consequence of some morbid change in the tissue in which they lie; they are common in parts

that have undergone atrophy or shrinkage. It almost appears as if the capillaries were striving to fill up the space left unoccupied by the receding tissue (compare Art. 150 on the formation of cavernous angiomata in the liver). Similar ectases are found in new-formed tissue, whether inflammatory or neoplastic. In these cases it is generally the new-formed vessels which appear dilated. They have either been over-large from the beginning, or have been dilated by some not easily recognizable cause after their first formation.

The capillary ectases occasionally met with in the brain VIRCHOW believes (*Virch. Arch.* vol. 30, with cases) to be in part congenital, and so to be properly classed with the nævi; ROTH is of the same opinion. If this be so the specimen figured in Fig. 132 from a telangiectatic glioma might exemplify a congenital condition of the vessels, existing therefore before the development of the substance of the glioma; but of course the point cannot be finally decided (HESCHL, *Wiener med. Woch.* 1868).

The dilatation of the capillaries in atrophic or shrunken tissues and in new-formations is probably dependent on several factors. It is of course a necessary condition that the capillaries shall always be full of blood; so that the shrinkage or atrophy must go on in such a way as not to exert pressure on the capillaries and so to empty them.

306. Dilatations of the veins are described as **phlebectases** or **varices.** They are very common, and occur chiefly as a consequence of mechanical hindrances to the emptying of the veins. Thus they are met with in connection with local or general engorgement, compression of the veins, venous thrombosis, imperfect action of the heart, etc. Their formation is favored by unhealthy conditions of the vessel-walls or their surroundings.

In accordance with their mode of genesis we find them occurring chiefly in places where the venous circulation is normally placed at a disadvantage, especially therefore in the lower half of the body. Their development may constantly be watched during life in connection with the veins of the legs and anus.

The cutaneous veins are either dilated uniformly and over a considerable extent, or bulged into fusiform or irregular sacculations. They are often at the same time elongated and convoluted, the bends of the convolutions being saccular. If two such sacculations are in contact, the vessel-walls may became adherent at the point, and the intervening tissue gradually disappearing by absorption, a new opening may be established between the two. Cavernous sinuses are thus formed, especially in the anal region: they form livid saccular tumors on the hæmorrhoidal veins surrounding the anus, and are referred to as **hæmorrhoids** or **piles.**

Varices affecting the internal organs are most frequently met with in those of the pelvis. **Varicocele** is a dilated and tortuous condition of the veins of the spermatic cord, occurring more frequently on the left side than on the right.

Varices are often not without danger to the patient, especially if they

exist in regions exposed to mechanical injury. Hæmorrhoids are often subject to rupture and hæmorrhage, as well as to inflammation (periphlebitis). Such inflammation may lead to fibrous hyperplasia or to abscess; the latter when bacteria settle in the inflamed tissues. Varicose patches of skin are especially apt to become inflamed on slight occasion, and in this way troublesome and indolent ulcers are produced. These are known as **varicose ulcers.**

Thrombi often form in dilated veins, and when they become calcified constitute the so-called vein-stones or **phleboliths.** In other cases the thrombi disintegrate and give rise to embolism. At times the thrombus becomes organized; the vein is filled up with fibrous tissue, and transformed into an impervious cord.

307. The processes by which arteries and veins may become narrowed or obliterated have already been more than once referred to under obliterating arteritis and the organization of thrombi. These play the chief part in the occlusion of the larger vessels, by setting up thickening of their walls or development of new tissue in their interior; in the smaller vessels they may lead to the conversion of the patent channel into an impervious fibrous cord.

Vessels are thus occluded by changes in their walls or in their contents; but they may likewise become narrowed or obliterated by compression from without, or by morbid processes affecting the tissues in which they lie. The veins are especially liable to such accidents: by the formation and contraction of cicatricial tissue around them large veins, even the vena cava, may be completely obliterated.

See EPPINGER (*Die narbige Obliteration der Vena cava inferior, Prag. med. Woch.* 1876).

CHAPTER XVII.

RUPTURE OF THE COATS OF THE VESSELS.

308. Aneurysms and varices may burst (Arts. 304 and 306), and this is the commonest cause of spontaneous hæmorrhage. But rupture may also occur in undilated vessels, when inflammatory and degenerative changes have reduced the natural resisting power of their walls. Lastly, various forms of injury may bring about the rupture of healthy vessels. Simple increase of blood-pressure does not lead to rupture in vessels that are really healthy.

When an artery gives way the ensuing hæmorrhage is great; it continues until the pressure of the blood accumulating in the tissues is as great as that within the bleeding vessel. The mass of gore and infiltrated tissue produced when the extravasated blood coagulates is called an **arterial hæmatoma.**

The rent in the vessel is closed by an aggregation of cohering white blood-cells, which solidifies into a colorless button-shaped plug projecting inwards and outwards from the plane of the rent (SCHULTZ). The plug within the vessel is after a time partly absorbed, and bulged outwards by the pressure of the blood. A sac is thus formed the interior of which communicates with the lumen of the vessel, while the exterior wall is mainly formed by colorless fibrin and the clots resulting from the primary hæmorrhage. Such a sac is called a **false or spurious aneurysm;** and is distinguished from a true aneurysm by the fact that the coats of the vessel form no part of its wall. If plastic inflammation is set up owing to the presence of the clots, an external sac-wall of granulation-tissue may be formed, and this may develop into cicatricial tissue. The fibrinous sac of the false aneurysm may give way again and lead to fresh hæmorrhage. In other cases the rent in the vessel is effectively closed by the transformation of the fibrinous plug itself into fibrous tissue. According to SCHULTZ this transformation is due to the white blood-cells which lodge in the cavity of the sac, and assume the functions of formative cells. White blood-cells likewise lodge in the meshes of the fibrinous sac-wall, and develop into large and active formative cells; these presently get the upper hand as it were, and the fibrin gradually disappears. Fibrous tissue is developed, and new vessels are formed in it, connected partly with the lumen of the old vessel and partly with the

vessels of the neighboring parts. The wall of the vessel itself takes no active part in the process; while the clots lying around it are absorbed.

Wounds of veins heal in the same way as those of arteries; it is rare for a sac or **false varix** of any size to be formed.

See KLEBS (*Beiträge z. Anatomie d. Schusswunden* 1872); CZERNY (*Virch. Arch.* vol. 62); SCHULTZ (*Deutsch. Zeitsch. f. Chir.* IX); PFITZER (*Virch. Arch.* vol. 77); HOLMES (*Syst. of Surgery* III. London 1883); BARWELL (*Intern. encyc. of Surg.* III. London 1883).

309. Sometimes, in consequence of disease or injury of one or other of the arterial coats, the inner and middle coat give way, while the adventitia resists the stress of the blood pressure. The result is that the blood does not at once escape out of the vessel, but strips the middle coat away from the adventitia. A blood-tumor is thus formed which is called a **dissecting aneurysm**. This variety of false aneurysm is chiefly met with in the ascending aorta, and in the smaller arteries of the brain. In the latter case, spindle-shaped dilatations are produced, which are bounded externally by the adventitia while the tube formed by the intima and media runs through the axis. In the case of the aorta, the adventitia is generally stripped loose over a considerable extent. The stress of the blood may indeed separate the adventitia from the other coats throughout the entire length of the aorta, and up the larger trunks, the dissection being only limited by the vessels passing into tissues which bind them down with some firmness. The mass of blood thus intruded between adventitia and media may be of quite remarkable thickness.

See PEACOCK (*Path. of the heart and arteries* Edinburgh 1849); FRIEDLÄNDER (*Virch. Arch.* vol. 78); FAGGE (*Med. chir. Trans.* 1869, with cases).

310. The **varicose aneurysm** deserves special mention. It is occasionally produced by the adhesion of a true aneurysm to a vein, the adhering tissues of the walls becoming gradually absorbed, so that a free communication is at length formed between artery and vein. In other instances, a false aneurysm may become connected with a vein, as when an artery and vein are simultaneously wounded by the same puncture. A true aneurysm intervenes between the two vessels in the former case, a false aneurysm in the latter case; we must thus distinguish true varicose aneurysm from false varicose aneurysm.

311. Occasionally, as the result of a wound we may have a direct connection of the channel of an artery with that of a vein, so that arterial blood pours into the vein without passing through an aneurysmal sac at all. This condition has been described as **aneurysmal varix**. The pressure of the arterial blood gradually dilates the vein, giving it a varicose appearance, and if the condition persists, its wall may become notably thickened.

The non-traumatic forms of varicose aneurysm specially affect the great vessels of the thorax; the traumatic form generally occurs between

the median basilic vein and the brachial artery, at the spot where bleeding from the arm is practised.

312. The **vascular neoplasms**, or tumors in whose structure the blood-vessels play an essential part, have already been discussed in the General Pathological Anatomy. Of this class the angiomata (Arts. 149, 150), the angiosarcomata (Art. 161), and the cylindromata (Art. 163) are the chief species.

Tumors of all kinds may, of course, involve the walls of the blood-vessels in their growth. The adventitia is specially liable to be implicated in carcinomatous or sarcomatous proliferation. The media and intima resist the invasion longer, especially in the case of the arteries; the veins are less resistant. The walls of the veins are often broken into by cancerous growths, so that tumor-particles gain entrance to the blood-current; and in this way cancerous thrombosis is set up. If tumor-germs are swept off from the thrombi, they may give rise to metastatic growths at some other point of the vascular system where they lodge.

CHAPTER XVIII.

THE LYMPHATICS.

313. The **morbid changes** occurring **in the lymphatic system** do not admit of complete treatment apart from that of the various organs. The lymphatics have their ultimate radicles in the very substance of the tissues; and arise in the natural meshes and lacunæ which exist in them. Into these meshes or lymph-spaces passes the liquid transuded from the blood-vessels; the meshes being continuous with lymph-channels, which are devoid of special walls and are only marked off from the parenchyma of the tissues by a layer of endothelial cells. These channels are the radicles of the lymphatics, and are abundant wherever connective tissue is found.

It must be very rare for demonstrable changes to take place in these minute lymph-channels without simultaneous disease of the tissues that enclose them; they and the tissues are in too intimate relation for one to suffer without the other. The same holds even for the larger lymphatics, though they have walls of their own in addition to the endothelial lining; it is indeed only the largest lymphatics of all that give marked evidence of their independence.

314. The lymphatics are not frequently inflamed, an affection described as **lymphangitis,** but more properly **perilymphangitis.**

It is generally secondary to some inflammation of the tissues; the lymph from the inflamed area acting as an irritant on the vessels through which it flows and on the tissues which environ them. It is rare for an irritant capable of setting up inflammation to reach the lymphatics from any other source than from a previously inflamed part. The secondary inflammation may extend far beyond the seat of the primary affection: thus it may reach from a wound in the hand up into the lymphatics and glands of the axilla. During life the affection is recognizable by the existence of red and painful streaks extending from the initial wound to the nearest lymphatic glands.

Minor degrees of inflammation are hardly if at all to be recognized *post mortem*, the redness generally disappearing soon after death; only when the lymphatics and their contents and surroundings have undergone considerable inflammatory change are the traces plainly visible. Under the microscope however it is not all difficult to make out the

inflamed lymphatics which ramify from the neighborhood of an inflamed area.

The histological changes associated with lymphangitis are mainly these:—the contents of the lymphatics are much more abundant, and much richer in cells, than normal lymph; it is often purulent in appearance; in other cases it is fibrinous or fibrino-purulent; where the inflammation is purulent the endothelium of the lymphatics is shed or disintegrated, in milder forms it is swollen and protuberant; occasionally subdivision of nuclei and cells is observed; the tissues surrounding the vessel, and the vessel-wall, are inflamed with migrated cells, and the blood-vessels are congested; only in the mildest cases of all is the change limited to swelling and desquamation of the endothelium.

The outcome of lymphangitis is either complete restoration *ad integrum* by re-absorption of the exudation and regeneration of the lost endothelium, or necrosis and abscess of the vessel and the tissue surrounding it, or lastly fibrous hyperplasia and induration of both. The latter occurs in chronic inflammatory conditions, and may lead to the obliteration of the vessel.

The infective granulomata may invade the lymphatic system, and the lymphangitis set up often exhibits no special peculiarities; but actual granulomatous change may likewise be induced, and then exhibits its specific characters. In this respect tuberculosis is the best example, as the affection is propagated with special readiness by way of the lymphatic vessels (Art. 122.)

References on lymphangitis and the associated changes:—VIRCHOW, *Virch. Arch.* vol. 23; LÖSCH, *ibid.*, vol. 44; BAUMGARTEN, *Cent. f. d. med. Wiss.* 3, 1882, with further references. On tuberculous disease of the lymphatics see KLEBS (*Virch. Arch.* vol. 44); LÉPINE (*Arch. de physiol.* 1870); PONFICK (*Berl. klin. Woch.* 1877); WEIGERT (*Virch. Arch.* vol. 88).

315. Inflammatory processes affecting the wall of a lymphatic and the surrounding tissue, pressure from without, the eruption of tumors or parasites into the channel, and other like causes, may bring about the **occlusion** of the vessel. If the number of lymphatics thus obliterated is not great, while other vessels remain open so that the lymph of the part can find an exit, no further change is usually induced. Even the thoracic duct may be occluded without serious danger, for other collateral paths are opened up. But if the efflux of lymph is entirely prevented, as in filarial disease (Art. 235), engorgement of the vessels with lymph ensues and the lymphatics become gradually dilated, forming what is called **lymphangiectasis.** This affection may however develop without demonstrable impediment to the outflow of lymph, generally in connection with repeated attacks of local hyperæmia or inflammation, but at times also without any such apparent cause.

Lymphangiectasis following parasitic obstruction and inflammation is chiefly observed in the form of cutaneous and subcutaneous hyperplasia

known as **elephantiasis.** The skin is thickened and on section allows an abundance of clear lymph to escape from the dilated lymphatics. The degree of the dilatation varies of course in different cases: sometimes the epidermis is raised in blisters and bullæ by the accumulated lymph.

Dilated chyliferous lymphatics are very often met with in the mesentery: the usual cause is obstruction due to inflammatory or neoplastic growths seated in the mesentery or thoracic duct. Sometimes the obstruction is due to lymphatic thrombosis. The dilated vessels look like straight cylindrical ridges or convoluted saccular or beaded cords; their contents are either white and limpid or pulpy and caseous.

Lymphangiectases, not associated with engorgement or inflammation, are generally congenital or depend on congenital defects. The affection known as lymphangiectatic **macroglossia** and **macrocheilia,** a peculiar overgrowth of tongue and lips, is due essentially to dilatation of the lymphatics of the parts. Lymphangiectases of the skin such as are often met with in the inguinal region, scrotum, labia pudendi, and on the thorax, are of the same nature. They sometimes form circumscribed tumor-like swellings and are hence classed with tumors as lymphangiomata (Art. 152). It is not possible to draw a sharp line between the swellings which we may fitly call tumors and the others.

The rupture of lymphatics and lymphorrhagia have been referred to in Art. 31.

On the consequences of closure of the thoracic duct see HELLER (*Deutsch. Arch. f. klin. Med.* x.); TURNER (*Edin. med. Journ.* 1859); STILLING (*Virch. Arch.* vol. 88).

On lymphangiectasis and lymphorrhœa see Arts. 31, 152; GEORJEVIC (*Arch. f. klin. Chir.* XII.); PETTERS and KLEBS (*Prag. Vierteljahrsschr.* 125); MANSON (*Med. Times and Gaz.* 2, 1875, and *The Filaria sanguinis hominis* London 1883); WIENKOWSKI (*Wien. med. Woch.* 33, 1877); DÉSERT (*Des dilatations lymphatiques,* Thèse de Paris no. 131, 1877); LESSE (*Ludwig's Arbeiten* 1872); QUINCKE (*Arch. f. klin. Med.* XVI., with references to cases); NIEDEN (*Virch. Arch.* vol. 90); WEGNER (*Arch. f. klin. Chir.* XX.); LEWINSKI (*Virch. Arch.* vol. 91). On macroglossia see BARKER (*Holmes's Syst. of Surgery* II. London 1883, with references).

316. In addition to the lymphatic tumors described as lymphangiomata we have a class of growths specially affecting the lymphatic vessels, and known as **endotheliomata** or **endothelial cancers.** They have been described chiefly as tumors of the serous membranes, of the pia mater, and of the skin; and they are either flattened and diffuse, or circumscribed. According to the principles already laid down (Art. 166), they are to be reckoned as sarcomata, characterized by endothelial proliferation and by the formation of peculiar nests and clusters of cells lying in a kind of fibrous stroma; the structure thus resembles in many points that of carcinoma. But it must be noted that many tumors described as endotheliomata have been really genuine carcinomata, which had irrupted into the lymph-channels. This is true of many of the so-

called endotheliomata not only of the skin but also of the serous membranes (Art. 358).

The endothelial cells of the lymphatics may take part in the growth of any of the connective-tissue group of tumors; but they do not give rise to any special peculiarities of structure.

The lymphatics very frequently participate in the growth and **propagation of the epithelial neoplasms.** This is notably the case with regard to carcinoma, which often breaks into the lymph-channels and there forms cancerous nodules and bands. Thus from a mammary carcinoma infection may spread to the lymphatics, not merely of the neighboring surface tissues, but even of the pleura and subpleural connective tissue. In this way long trains and cluster of cancer-nodules may be formed following the lines of the pleural lymphatics. The share taken by the endothelial cells in the process of propagation is still under discussion. Many are of opinion that they give rise to cancer-cells. This is very far from being demonstrated, but it is perhaps possible. The author has observed in some instances that the endothelial cells were proliferous, but has no evidence that they became transformed into cancer-cells. Meanwhile it is probably true that if they produce tissue at all, it is fibrous tissue; that is to say they give rise to cancer-stroma, not to cancer-cells.

On endothelioma see Art. 161; Köster (*Die Entwickelung d. Carcinome* 1869); Pagenstecher (*Virch. Arch.* vol. 45); Eberth (*Virch. Arch.* vol. 49); Arndt (*ibid.* vol. 51); Perls (*ibid.* vol. 56); Waldeyer (*ibid.* vol. 55); Wagner (*Arch. d. Heilk.* (1870) XI.); Neelsen (*Arch. f. klin. Med.* XXX., with cases and references).

SECTION III.

THE SPLEEN AND THE LYMPHATIC GLANDS.

CHAPTER XIX.

STRUCTURE AND FUNCTIONS OF THE SPLEEN.

317. **Structure of the spleen.** The spleen plays a peculiar and important part in connection with the elaboration and metabolism of the blood; and its relation to the blood accounts in some measure for its anatomical structure and for its special relation to the vascular mechanism. The proper or characteristic tissue of the spleen is the pulp, and this is so intimately connected with the vascular system that its interspaces constantly contain both the fluid and the corpuscular elements of the blood in abundance. The volume of the adult spleen is from 150 to 180 ccm.

The **spleen-pulp** consists of a delicate membranous reticulum or 'honeycomb' traversed by stouter strands or trabeculæ originating in the capsule or in the fibro-cellular (lymphadenoid) sheaths that ramify with the vessels from the hilum. The interspaces of the reticulum are in communication with wide, thin-walled capillaries and veins deriving their blood-supply from the arteries, which enter at the hilum and bifurcate dichotomously into minute arterioles. The capillaries of course intervene between the arterioles and the radicles of the veins. It has been shown that the capillary-walls are not continuous but interrupted, so that blood can permeate freely the meshes of the pulp. And even if, as some maintain, there are no easily-visible clefts or pores in the vessels, it is at least certain that the walls are in so far more pervious than the walls of other vessels that the corpuscles pass through them with great ease, and that the mass of the pulp is in part made up of blood-cells. The reticulum contains lymphoid cells, larger round colorless cells with one or more nuclei, and ordinary red corpuscles, together with corpuscle-carrying cells, pigment-granule cells, and free yellow or brownish pigment. This pigment in conjunction with the blood gives the spleen its brownish-red color.

The spleen contains besides certain special structures known as **malpighian follicles** (or corpuscles). They are composed of lymphadenoid tissue, continuous with the cellular connective tissue sheathing the arteries and forming indeed but a modification of it. They contain colorless cells only, and their blood-vessels are narrow capillaries, which unite and open into wide venous channels or sinuses at the periphery of

the follicles. The color of these lymphoid follicles is therefore pale or grayish-white.

The capsule and the trabeculæ contain numerous unstriped muscular fibres, which are arranged with some regularity.

The outer form of the spleen is somewhat variable, but it is generally more or less flattened or tongue-shaped. It is often remarkably lobulated, or at least deeply indented. Small detached **spleniculi,** from the size of a bean to that of a hazel-nut, are occasionally found near the spleen. Misplacements of the spleen are common, and it is occasionally wanting altogether.

318. The **functions of the spleen** are as yet imperfectly ascertained. It is very probable that the red corpuscles are broken up within its meshes; that is to say that worn-out or useless red corpuscles pass into the splenic tissue (Art. 268) and there undergo further changes. According to QUINCKE and KUNKEL a part of the iron contained in the red corpuscles which are disintegrated is utilized in the formation of new ones, while another part passes into the liver for elimination. Recent researches have thrown doubt on the formerly-accepted theory that red corpuscles are manufactured in the spleen itself. The most recent investigators are divided on the question, NEUMANN being against the older view, and TIZZONI for it. BIZZOZERO rejects altogether the idea that blood is normally manufactured in the spleen after the close of the fœtal period; but he thinks the spleen may resume such a function in certain peculiar conditions, as in anæmia. So much at least is sure, that the red corpuscles met with in the splenic pulp are not new-formed, but have escaped from the blood-vessels; and that they either return to the blood after undergoing some alteration, or are destroyed. If new cells are furnished to the blood by the spleen at all, they are colorless cells derived from the lymphadenoid sheaths of the arteries.

The view that the worn-out and useless red corpuscles are brought to the spleen and there broken up is supported by pathological facts. When the disintegration of red corpuscles in the blood is by any cause (such as malaria, Art. 268) increased, the number of cells containing red corpuscles and pigment, and the amount of free pigment, in the spleen is likewise increased. The organ may indeed become thereby stained of a deep russet or slate color. We may suppose that the increased disintegration sets free more pigmentary matter that can be utilized in the formation of new corpuscles or eliminated though the liver, and so it accumulates in the spleen.

Foreign matters circulating in the blood are specially apt to be deposited in the spleen (Art. 266): it is clear that the diminished current in the wide capillaries and veins, and their pervious walls, greatly favor such deposition.

On the structure of the spleen see KLEIN (*Quart. J. micro. sci.* 1875, ***Atlas of Histology London*** 1880).

The more recent researches on the functions of the spleen have been those undertaken by NEUMANN (*Arch. d. Heilk.* XV., *Berl. klin. Woch.* 20, 1880, *Zeitschr. f. klin. Med.* III.), FOÀ and SALVIOLI (*Arch. p. l. scienze med.* IV.), BIZZOZERO (*ibid.* I., *Arch. ital. de biol.* I.), TIZZONI (*Acad. dei Lincei* X. Ser. 3, *Arch. ital. de biol.* I.), KORN (*Virch. Arch.* vol. 86), ROY (*Camb. Journ. of Physiol.* III.), WINOGRADOW (*Cent. f. d. med. Wiss.* 50, 1882). NEUMANN pronounces definitely against the view that during extra-uterine life the spleen takes any part in the elaboration of the blood. BIZZOZERO, FOÀ, and SALVIONI are of opinion that after serious hæmorrhage the spleen does aid in manufacturing new blood. TIZZONI likewise thinks that blood may not only be destroyed but produced in the spleen; resting his opinion on the results of extirpating the spleen in dogs. The proportion of hæmoglobin in the blood rises shortly after the operation ; in about two days it returns to the normal, and then sinks more or less below it, to rise again after a certain interval. The last effect is due to the fact that not only is the blood-destroying function of the bone-marrow increased but also the blood-producing function. He finds that extirpation is occasionally followed by reproduction of splenic tissue in the form of numerous (60 to 80) nodules lying in the omentum, and more sparsely in other parts of the peritoneum. These cellular nodules when mature consist of malpighian follicles, pulp, and a capsule ; and they may coalesce into larger masses. They contain young nucleated red corpuscles. FOÀ disputes TIZZONI'S account of the structure and function of these nodules, and does not believe that they have any relation to the presence or absence of the spleen (*London med. Record* July 1883). ROY has discovered that in health the spleen expands and contracts rhythmically by means of the muscular tissue contained in its capsule and trabeculæ ; and he believes that the circulation of the blood through the organ is maintained not by the general blood-pressure but by the force of these rhythmical contractions.

CHAPTER XX.

DISORDERS OF CIRCULATION AND INFLAMMATIONS OF THE SPLEEN.

319. The amount of blood contained in the spleen is subject to considerable and incessant physiological variation. During digestion the organ increases in size from congestive hyperæmia, which passes away as the blood-supply diminishes on the contraction of the afferent arteries; the reduction in size being further aided by the tension of the elastic fibres and the contraction of the unstriped muscular fibres of the trabeculæ and the capsule.

Congestive hyperæmia may in like manner occur as a morbid condition exceeding the physiological condition in intensity and duration. In all the infective disorders of the system, as in typhoid and other acute exanthemata, in syphilis and in pyæmia the onset of the disease is accompanied by splenic hyperæmia. The spleen enlarges, and that in much greater proportion to its size than do the other organs which become hyperæmic at the same time: this is due to the fact that not merely are the capillaries and veins distended with blood, but also the mass of the splenic pulp which is in free communication with them. Such a spleen looks large and its capsule is tense; the pulp is deep red, and so soft that on section it may be easily scraped away. The malpighian follicles sometimes stand out distinctly as white nodules, sometimes are scarcely recognizable amid the swollen pulp.

320. The congestive hyperæmia may pass away rapidly, but it often persists for some time and further changes are set up in consequence. This is especially the case with the enlargement accompanying the acute infective diseases, such as typhoid, pyæmia, relapsing fever, ague, acute nephritis, and scarlatina. The spleen of a patient dead of typhoid at the beginning of the second week, or of septicæmia about the fourth or fifth day, appears not red but grayish or pale reddish-gray; its volume is greater than in simple congestion, reaching perhaps the double or the quadruple of its normal size. The pulp is extremely soft, almost diffluent, the softness being often however due in part to commencing putridity: in extreme cases the capsule may be so strained as to rupture.

In such a condition the spleen cannot be regarded as affected simply by excessive hyperæmia. The microscope shows that the vessels and

pulp are not distended with red cells as in hyperæmia, but that both contain an extraordinary number of white cells; and it is these that give the tissue its grayish tint. Whence they come is not easy to determine, though it is highly probable they reach the spleen by the channel of the circulation. Possibly too the production of lymphoid elements within the malpighian follicles may be abnormally increased; but the follicles show little or no sign of increase in size.

This form of enlargement of the spleen is in fact to be regarded as inflammatory, the evidence of a true **splenitis.** In support of this it may be mentioned that the exterior or capsular surface often shows signs of accompanying inflammatory change, such as turbidity of the capsule and deposits of fibrin upon it. It is of course more difficult to draw a hard and fast line between hyperæmia and inflammation in the case of the spleen than in other organs, for the spleen normally contains blood-cells which have escaped from the vessels.

The cells lying in the swollen grayish pulp are in part exactly like lymphoid elements, in part larger and with clear vesicular nuclei. A considerable number of the lymphoid cells contain red corpuscles or fragments of such in their interior; a sign that the destruction of red corpuscles is not only not diminished but actually increased.

As foreign matters circulating in the blood are apt to be deposited in the spleen, it is very probable that organized infective matters may in like manner tend to lodge there, and so lead to inflammatory vascular changes. Many such organisms are probably destroyed in the spleen. See BIRCH-HIRSCHFELD (*Arch. d. Heilk.* XIII.), FRIEDREICH (*Samm. klin. Vorträge* 75), SOCOLOFF (*Virch. Arch.* vol. 66), FISCHL (*Prag. med. Woch.* 1879), KLEIN (*Trans. Path. Soc.* 1877).

321. The **consequences** of congestive hyperæmia and inflammation of the spleen are various.

As the general disease passes away the infiltrative swelling of the spleen-pulp usually diminishes. The red and white blood-cells that remained lodged in the pulp are gradually passed on, and the spleen recovers its normal bulk and appearance. As the swelling declines cells may be found containing not only fragments of blood-cells, but also oil-globules; a sign that they are in process of decay.

In other cases the changes may be more permanent and assume the form of fibrous **hyperplasia** of the pulp, trabeculæ, vessel-walls, and capsule, together with enduring pigmentation. These changes are especially apt to occur when the hyperæmic condition recurs frequently (as in malaria), or when the inflammation takes on a formative or plastic character. Diffused or circumscribed thickenings then appear on the capsule, and may take the form of flattened lenticular nodules, or large dense cartilaginous patches. Occasionally the entire capsule is transformed into a coarse scar-like fibrous mass (BILLROTH, *Virch. Arch.* vol. 23; WILKS, *Trans. Path. Soc.* 1864).

Adhesions of the spleen to the surrounding structures in consequence

of inflammation (**perisplenitis**) are common ; false membranes may thus be formed uniting the spleen with the diaphragm, the splenic flexure of the colon, and the fundus of the stomach, and cause difficulty in dissecting out the spleen *post mortem*. But all such adhesions are not evidence of primary splenic inflammation ; inflammatory processes set up in the neighborhood of the spleen may induce secondary inflammation in the latter.

The appearance of the spleen varies in such cases ; it may be small and granular on the surface, or it may be considerably enlarged. The latter is notably the case in chronic malarial disease (**ague-cake**). The variety of size depends chiefly on the scantiness or abundance of the pulp ; but the trabecular frame-work may be hyperplastic and contribute to the general enlargement. The tint of the pulp also varies greatly. If it contains little or no pigment, it is bright red ; if pigment is abundant, it is brown or slate-colored. Its consistence is firm, so that on section it is not easy to remove the pulp by scraping. The number of lymphoid cells in the pulp is on the whole inconsiderable ; when pigment is present at all, these cells usually contain most of it in the form of yellow, brown, or black granules ; free pigment also occurs. The endothelial cells of the venules and some cells of the malphigian follicles likewise contain fine granules of pigment.

The trabeculæ are more or less thickened ; in marked cases the thickening may be recognizable by the unaided eye. It is only in very firm or hard spleens that the finer reticulum of the pulp is sensibly thickened. The walls of the arteries and veins are likewise thickened and pigmented, the pigment lying free in the walls or enclosed in cells. The changes in question are exhibited most markedly by patients who have suffered from malaria, but they are also met with in connection with other affections, such as typhoid. The pigmentary changes are due to increased destruction of blood-cells in the blood and the spleen.

322. Inflammation of the spleen rarely passes into **suppuration.** When it does the colorless cells accumulate in the pulp and follicles in great numbers, giving the whole tissue a yellowish-white tint. In very rare cases the entire substance suppurates ; the spleen being changed into a gray or grayish-red creamy mass. Circumscribed suppurations are commoner. The tissue about to break down takes on a grayish or yellowish-white color, and then becomes diffluent or liquid, forming **splenic abscesses.**

These occur chiefly in pyæmic affections, and in relapsing fever (PONFICK); that is to say in affections depending on bacterial invasion of the blood.

The tissue around a splenic abscess is generally discolored and infiltrated with pus; it is less usual for the abscess to be shut off by an enclosing membrane of granulation-tissue. The abscess often breaks through the capsule; and should the pus enter the peritoneal cavity,

fatal peritonitis ensues. But if adhesions have previously been set up between the spleen and the stomach-wall or diaphragm or colon, the abscess may break into the stomach or thorax or intestine.

See BESNIER (Art. *Rate* in *Dict. encyclop. d. sciences méd.*), PONFICK (*Virch. Arch.* vol. 60), MOSLER (*Ziemssen's Cyclop.* VIII.), WARDELL (*Reynolds' Syst. of Med.* V.).

323. **Passive hyperæmia** of the spleen follows upon such disorders of the circulation as interfere with the flow of blood through the splenic vein. Such are affections of the liver on the one hand, of the heart and lungs on the other. Cirrhosis of the liver is the chief of the former class, inasmuch as it often leads to the obliteration of the greater number of the portal capillaries within the liver.

When engorgement of the spleen has persisted for some time, the organ is usually found to be either normal in size or somewhat enlarged; it is rarely diminished. It is commonly more cup-shaped than in health, and the edges are more rounded. It is always firmer and sometimes actually hard, owing to the density of the pulp, which may be bright-red or dark in color. Hardly any of the pulp can be scraped off from the section; the trabeculæ stand out sharply; and the capsule is often thickened. The chief textural alteration in such a spleen is the increased amount of fibrous tissue it contains, the increase appearing in the trabeculæ and in the walls and sheaths of the vessels. The venous sinuses are of course dilated. Occasionally the reticulum of the pulp is found to be slightly thickened.

Anæmia of the spleen, such as follows upon great hemorrhage, is manifested by the very pale color of the tissue.

324. **Embolic infarctions** of the spleen, or the cicatrices to which they give rise, are very often to be observed in the post-mortem room. The emboli are generally derived from endocarditic vegetations or from thrombi of the heart or aorta. The infarcts are of various sizes; small ones may be as large as a cherry, larger ones may extend over as much as a half or more of the whole spleen. In the early stages of their existence they appear as pale yellowish (anæmic) or dark-red (hæmorrhagic) wedge-shaped patches with the base outwards, and on section project above the general level; in the hæmorrhagic patches the decolorizing process begins almost at once. The infarcts which one generally sees are either of one color throughout, or the centre is pale while the margin remains dark. When decolorization is well begun, the centre is brownish-red or orange or opaque gray or yellowish-white; the marginal zone, if there is one, will then be dark-red.

When the red or hæmorrhagic infarct is examined under the microscope it is seen that the veins, capillaries, and pulp are all distended with blood. The follicles are hæmorrhagic only at their margins, the centres being unstained. In decolorized infarcts the red corpuscles appear in part disintegrated, and in part distorted and discolored. The nuclei of the tra-

beculæ are no longer visible, the trabeculæ themselves being swollen and beset with oil-globules. The lymphoid elements are either gone, or in process of breaking up into granular and fatty detritus, and few nuclei are visible. At a later stage the reticulum and cells are alike transformed into a granular mass, in other words the entire tissue has perished by necrosis. Traces of the normal structure remain only in the marginal zone of the infarct, in which staining reagents still bring out the nuclei of the cells and the trabeculæ.

Plastic inflammation of the surrounding spleen-tissue accompanies the necrosis, a congested zone of demarcation is formed, and the necrotic mass is by degrees re-absorbed. After a time a dense shrunken radiating cicatrix is formed in the site of the infarct; it is often pigmented, or flecked with shining white spots. Large infarcts are sometimes imperfectly reabsorbed, so that the cicatrix encloses a necrotic caseous patch. If bacteria or other septic virus reach the seat of infarction, purulent or putrid inflammation may be set up instead of the changes just described.

See BILLROTH (*Virch. Arch.* vol. 23), COHNHEIM (*Untersuch. üb. d. embol. Processe* Berlin 1872), LITTEN (*Untersuch. üb. d. hæm. Infarct.* Berlin 1879), GUILLEBEAU (*Die Histologie d. hæm. Infarcts* In. Diss. Berne 1880), WEIGERT (*Virch. Arch.* vol. 79), HAMILTON (*Liverpool med.-chir. Journ.* 5, 1883; the existence of the red or hæmorrhagic form is questioned), ORTH (*Lehrb. d. spec. path. Anat.* I. Berlin 1883; the larger infarcts are stated to be nearly always of the anæmic form). English authors generally refer to such infarcts as fibrinous blocks or deposits.

CHAPTER XXI.

DEGENERATIONS AND INJURIES OF THE SPLEEN.

325. **Simple atrophy** of the spleen occurs chiefly in aged or marasmic patients, especially in case of long-standing anæmia. The organ is small, the capsule wrinkled and sometimes thickened. The pulp seems loose and pale; and the trabeculæ stand out sharply. Under the microscope the cells of the pulp are seen to be scanty and the blood-vessels imperfectly filled.

Amyloid degeneration is the most notable of the retrogressive processes affecting the spleen; two forms of amyloid spleen are distinguished—the 'sago' spleen, and the 'bacon' spleen.

In the **sago spleen** the malpighian follicles are the seat of the amyloid change. The spleen is generally somewhat enlarged and firmer than is normal. In the brownish- or grayish-red pulp lie light-brown hyaline translucent grains like boiled sago, somewhat larger than the normal follicles. When dilute solution of iodine is poured over the previously-washed surface, the grains become deeply stained of a brownish-red color: a section steeped for a short time in methyl-violet and then washed in alcohol containing a little hydrochloric acid shows the grains red on a bluish ground.

The uniformly lardaceous or **bacon spleen** is in general very considerably enlarged, and firm and resistant to the touch. On section the pulp shows diffuse or continuous patches which are hyaline or translucent, resembling somewhat the fat of fried bacon. Sometimes the greater part of the pulp is thus transformed, the normal tissue appearing in scattered islets only.

The amyloid change mainly affects the trabeculæ and the walls of the venous sinuses. The lymphoid elements of the follicles and the pulp-cells are affected secondarily. Amyloid trabeculæ swell up greatly and become nodulated or varicose. The cells lying in the interstices become atrophied and so perish; it is possible that some of them may be transformed into amyloid substance. Arteries whose lymphoid sheaths are degenerate may themselves either be free from change, or may degenerate in like manner. When the pulp becomes amyloid the walls of the capillaries and venules become thickened and degenerate.

See VIRCHOW (*Virch. Arch.* vol. 8), KYBER (*ibid.* vol. 81, with references), EBERTH (*ibid.* vols. 80, 84).

326. **Rupture** of the spleen may occur spontaneously when the organ becomes abnormally enlarged. Traumatic rupture is more common, and may occur in a healthy spleen or in one which has already undergone morbid change. Ruptures of any considerable size are followed by very grave hæmorrhage. If the hæmorrhage is stayed by the formation of a thrombus filling the rent, the wound may heal as in other organs; the clot is gradually absorbed and a scar takes its place. The same process takes place in other wounds of the spleen. Death sometimes ensues not from primary hæmorrhage but from suppurative inflammation set up in the wounded tissue.

CHAPTER XXII.

INFECTIVE GRANULOMATA OF THE SPLEEN.

327. **Tubercle** is very frequently found in the spleen. In attacks of general miliary tuberculosis miliary tubercles are nearly always developed both in the parenchyma and in the capsule. In chronic tuberculosis such tubercles as may happen to be produced in the spleen give rise to caseous nodes of various sizes. The tubercles are seated in the malphigian follicles, in the lymphoid sheaths of the vessels, and in the pulp. They may consist entirely of small cells or be caseous in the centre, according to their age.

Gummata rarely develop in the spleen, though they are sometimes met with in both congenital and acquired syphilis. They may be single or multiple, and form gray and translucent or yellow and opaque nodes with grayish margins, according to their age. The grayish margin consists of cellular granulation-tissue, which is stained intensely with coloring reagents, and passes gradually into the normal tissue of the pulp.

Syphilis may also manifest itself by a general **hyperplastic enlargement** of the spleen, which is observed mainly in the congenital form of the disease. The spleen of a new-born infant weighs about nine grammes or 0.3 per cent of the body-weight; in syphilitic infants the average weight of the spleen is, according to BIRCH-HIRSCHFELD, some fourteen grammes or 0.7 per cent of the body-weight. Its stroma is increased in amount, and the sheaths of the arteries infiltrated with cells. BIRCH-HIRSCHFELD found oil-globules and pigment-granules in the constituent cells of the pulp.

On syphilis of the spleen see WEIL (*Arch. f. klin. Med.* XIII.), WEVER (*ibid.* XVII.), BÄRENSPRUNG (*Die hereditäre Syphilis* Berlin 1864), WAGNER (*Arch. d. Heilk.* IV.), MOSLER (*Berl. klin. Woch.* 1864), GEE (*Brit. Med. Journ.* 1, 1867), GERHARDT (*Lehrb. d. Kinderkrankh.*), BIRCH-HIRSCHFELD (*Arch. d. Heilk.* 1875 and *Gerhardt's Handb. d. Kinderkrankh.* IV.), BÄUMLER (*Ziemssen's Cyclop.* III., for further references), TEPEL, (*Path. Anat. d. hered. Syph.* In. Diss. Berlin, 1874), BARLOW (*Path. Soc. Trans.* 1877).

CHAPTER XXIII.

HYPERPLASIAS AND TUMORS OF THE SPLEEN.

328. We have already (Art. 321) referred to various forms of enlargement of the spleen associated with acute infective diseases. Such enlargements are partly due to an increase of the pulp, and partly to an increase in the fibrous framework. But there is another and very important form of **splenic hyperplasia**, whose ætiology is altogether obscure, although it constitutes a grave disease.

This form of hyperplasia usually extends over the entire spleen; it is rarely limited to isolated patches. So far as is known the affection commences with an increase of the parenchyma as a whole, the constituent elements undergoing a general hyperplasia. The tissue is bright-red and soft, while the follicles are not separately distinguishable. In a much rarer form of the disorder the malpighian follicles become hypertrophied, and stand out as grayish nodules or in white lobulated clusters.

As the parenchyma increases in size the originally soft tissue becomes firmer, and at the same time paler. The follicles are often still unenlarged, but they may at this stage become hypertrophied and form whitish nodes and clusters of considerable size. The capsule is in general somewhat thickened and beset with coarse fibrous patches of various sizes; and adhesions are often formed with the surrounding organs. The enlargement thus brought about may be very remarkable, the weight of the spleen sometimes reaching three or four kilogrammes.

In the earlier stages the hyperplastic enlargement of the pulp and follicles, in so far as it is independent of the amount of blood present in the spleen, is due to an increase in the number of the constituent cells. When the follicles develop into nodes of any size they compress the spleen-pulp between them, and it often becomes atrophied in consequence. It is then found to contain fatty cells and pigment-granules either free or enclosed in other cells. The section thus assumes a delicately mottled and speckled appearance, the brown and yellow atrophied and pigmented pulp alternating with grayish and yellowish follicular nodules. The disorders of circulation consequent on these textural alterations often lead to the formation of hæmorrhagic infarcts, and these according to their age appear as red, brown, or yellow patches.

In old hyperplastic spleens the enlarged follicles are found to have lost their original structure, and form fibro-cellular masses without any clear traces of the reticular or lymphadenoid type. The pulp itself may become more or less fibrous.

The changes just described may occur primarily in the spleen, or may follow upon like changes in the lymphatic glands and bone-marrow (Art. 344). In the former case a similar affection of the lymphatic glands is associated with the primary affection of the spleen. Afterwards tumors consisting of lymphadenoid tissue may form in organs which normally contain none of it.

The splenic as well as the lymphatic hyperplasia is very often associated with leukæmia (Art. 260), and is therefore often referred to as **leukæmic hyperplasia.** If no leukæmia exists, the affection is described as **pseudoleukæmia or Hodgkin's disease,** or as splenic (or lymphatic) anæmia. The latter description refers to the fact that patients suffering from the affection become profoundly anæmic and ultimately die of anæmic exhaustion.

We know nothing of the cause of leukæmic or pseudoleukæmic hyperplasia of the spleen. In some cases the affection has been preceded by some form of injury or infective disease, in other cases there has been nothing of the kind. We are as little able to say whether or not the two forms are identical. Their identity would seem to be indicated by the fact that they show no anatomical differences, and that one form may pass into the other. The affection may occur at any age.

When the process begins in the lymphatic glands (as in so-called **adenia**) and attacks the spleen secondarily, it is the lymphoid follicles of the spleen which first exhibit a hyperplastic multiplication of their cells.

References:—Art. 344; HODGKIN, *Med. chir. Trans.* XVII. (1832); VIRCHOW. *Virch. Arch.* vol. 5, and *Gesamm. Abhand.* 1856; MOSLER, *Path. und Therap. d. Leukämie* Berlin 1872, with references to the earlier literature of the subject; PONFICK, *Virch. Arch.* vols. 56, 58; BIRCH-HIRSCHFELD, *Gerhardt's Handb. d. Kinderkrankh.* III.; COHNHEIM, *Virch. Arch.* vol. 33; TROUSSEAU, *Clinical Medicine* (New Syd. Soc.) V.; EBERTH, *Virch. Arch.* vol. 51; LANGHANS, *Virch. Arch.* vol. 54, CORNIL and RANVIER, *Man. Path. Hist.* I.; MURCHISON and SANDERSON, *Trans. Path. Soc.* 1869–70, with cases and references; GREENFIELD, GOWERS, *ibid.* 1878; WILKS, *Guy's Hosp. Rep.* 1865, *Lancet* 1, 1878.

329. If we leave out of account the hyperplastic enlargements of the spleen just described, which resemble the true tumors in several respects and especially in the occurrence of associated metastatic growths, we find that **primary neoplastic tumors** of the spleen are very rare. Fibroma, sarcoma, and angioma, have been met with. LANGHANS has described (*Virch. Arch.* vol. 75) a case where an injury was followed by the growth of a pulsating cavernous angioma of the spleen with metastases in the liver, the splenic growth occupying nine-tenths of the already greatly enlarged bulk of the organ. Dermoid tumors are likewise very rare. Cysts containing blood or serous liquid are sometimes met with.

Metastatic growths, especially carcinomata, are more common than

the primary forms; secondary carcinoma usually taking the form of rounded nodules.

Pentastoma (Art. 225) is the commonest of the animal parasites infesting the spleen. It forms nodes as large as a pea, which are usually calcified. Echinococci and cysticerci are also occasionally met with.

CHAPTER XXIV.

ATROPHY AND DEGENERATION OF THE LYMPHATIC GLANDS.

330. The **lymphatic glands** stand to the lymphatic system somewhat in the same relation as the spleen to the blood-vessels. The glands may be described as masses of lymphadenoid tissue (that is to say, of reticular fibrous tissue containing lymphoid cells in its meshes) aggregated here and there around the lymph-channels. They contribute to the lymph the lymphoid elements produced in their follicular meshwork, and perhaps exert upon it some chemical influence besides.

The lymph passing through the glands is derived from a threefold source. The chief source is the transudation from the blood. This permeates the tissues, giving up to them some of its constituents and taking up from them some products of their metabolism: while at many points of the body, and especially at the absorbing mucous surfaces, substances enter and mingle with the lymph which are originally derived from without the body.

From the normal sources of the lymph the lymphatic glands may in like manner receive noxious matters; and these may be such as to induce more or less grave disorders of function, and even of anatomical structure. Thus the lymphatic glands are liable to secondary disease, following upon primary disease of the tissues whence their lymph is derived.

In addition to these the lymphatic glands are subject to various forms of independent disease, which are partly retrogressive and partly progressive or constructive in their nature.

331. **Simple atrophy.** In advanced age the lymphatic tissues generally are observed to undergo senile diminution; the lymphatic glands become smaller, and the lymphadenoid tissue of the mucous membranes becomes scantier. The thymus gland, which is of the same nature, dwindles away in the early years of life.

The decrease in the volume of the lymphatic tissues is due to a diminution in the number of their lymphoid elements. In the case of the thymus these elements disappear wholly, and the remaining connective tissue becomes transformed into fat.

This general physiological retrogression may be imitated under morbid conditions, especially in the general marasmus of children; but

wasting of the lymphatic tissues may also follow upon localized disease. The mesenteric glands are those most apt to atrophy.

In such cases the lymphoid elements, and chiefly those of the medullary cylinders, are the first to disappear. Sometimes the lymphoid elements entirely disappear and the reticulum is changed into adipose tissue, beginning at the hilum. Atrophied lymphatic glands, if not morbidly pigmented, have a light gray tint and are usually firmer than is normal: when transformed into fatty tissue, the change is sufficiently apparent.

332. **Amyloid degeneration** of the lymphatic glands is a common affection. Usually other organs are affected by it at the same time; it is rarely confined to the glands alone. When it is, the cause is nearly always some chronic suppuration within the territory whence the lymph-

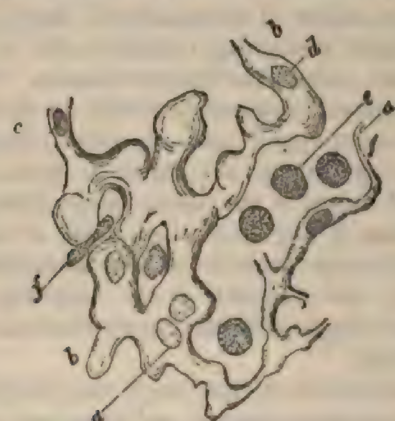


FIG. 133. AMYLOID SWELLING OF THE ADENOID RETICULUM.

(*After EBERTH: methyl-violet staining:* × 850.)

a, normal reticulum.
b, swollen reticulum.
c, unaltered nucleus.
d, degenerate nucleus.
e, normal lymphoid corpuscle.
f, atrophied lymphoid corpuscle.

supply of the affect glands is drawn. If the amyloid change is at all advanced it is often distinguishable by the dull grayish tint and firm consistence of the glands on section; to make certain however, we must employ the iodine or methyl-violet reaction, or examine the glands microscopically. When they are really amyloid the iodine brings out brownish-red flakes and patches in the lymphoid tissue or on the walls of the blood-vessels. Sometimes the sinuses are most affected: in other and more usual cases it is the follicles and interfollicular septa. The capsule is frequently more or less thickened.

When a markedly amyloid lymphatic gland is closely examined, it gives one the impression that the masses of amyloid substance are partly the lymphoid corpuscles transformed into shining blocks, and partly the reticulum and septa which have become swollen and hyaline. EBERTH

however has shown (*Virch. Arch.* vol. 80) that the lymphoid corpus es very rarely if indeed ever take part in the amyloid change. The shining amyloid blocks, which are of about the same size as the corpuscles, are really derived from the degenerate reticulum.

The process of degeneration begins with a hyaline thickening of the reticular trabeculæ (Fig. 133 *a*). Then the trabeculæ become nodulated (*b*) and form contiguous blocks or lumps. The nuclei of the reticulum (*c*) often remain unaltered for an astonishingly long time. They ultimately become very pale (*d*), cease to stain blue with methyl-violet, and then break up and disappear. The lymphoid corpuscles diminish in proportion as the reticulum thickens, and may here and there disappear entirely. In the larger vessels it is chiefly the media which is affected, in the capillaries it is the adventitia.

Hyaline degeneration of the lymphatic glands has quite recently been described by CORNIL; it has a certain resemblance to amyloid change but is essentially distinguished from it by the absence of the reaction with iodine and methyl-violet (Art. 63). The change in some instances affects mainly the blood vessels of the gland (WIEGER, *Virch. Arch.* vol. 78), which are transformed into hyaline tubes by the thickening of their walls and the narrowing of their channel. In other cases hyaline masses are formed from the reticular cells; the hyaline masses are probably related to the colloid substance (Art. 56). Their presence is recognizable by the whitish somewhat opaque trabeculæ which run through the grayish-red tissue of the gland. Calcification often sets in when the degeneration reaches a certain stage.

There is another variety of homogeneous degeneration which deserves mention. It is met with chiefly in glands which are the seat of larged-celled hyperplasia (Art. 340), or of tubercle (Art. 342). It was shown in Art. 39 that this variety of degeneration is closely allied to caseation (Art. 333). Some authorities (such as ARNOLD, *Virch. Arch.* vol. 87) see in it a special kind of degeneration, which only in its advanced stages leads to caseation.

Reference:—CORNIL, *Journ. de l'anat. et de la phys.* 1878; CORNIL and RANVIER, *Man. Path. Hist.* vol. I.; WIEGER, *Virch. Arch.* vol. 78; PETERS, *Virch. Arch.* vol. 87; VALLAT, *Virch. Arch.* vol. 89; VIRCHOW, *ibid.* vols. 85, 89.

333. **Fatty degeneration, calcification,** and **necrosis** of the lymphatic glands occur mainly as consequences of inflammatory disease. Fatty change and soft caseous necrosis are best exemplified in connection with the specific inflammations of scrofula and tuberculosis. A lymphatic gland already altered or enlarged, and it may be pigmented, exhibits on section one or more isolated caseous foci, or is transformed entire into an opaque white cheesy mass contained in a fibrous capsule. In later stages such glands may take up fluid and become diffluent or liquefied, or they may become calcareous.

The second or firm variety of caseous necrosis begins as a homogeneous degeneration. It occurs mainly in hyperplastic (Art. 340) and tuberculous (Art. 342) glands, which often have a glassy or translucent appearance even to the naked eye. The process is found on examination to start in a uniform or homogeneous transformation of the entire tissue,

or of single cells in it, which take the form of shining flakes or lumps and gradually lose their nuclei. If the tissue so changed passes on into the soft variety of caseation, it breaks up into a granular friable mass.

Necrotic patches, made up of grayish friable moist tissue, are formed in the glands generally after acute inflammatory swelling, such as often accompanies typhoid fever and diphtheria. The lymphoid cells are

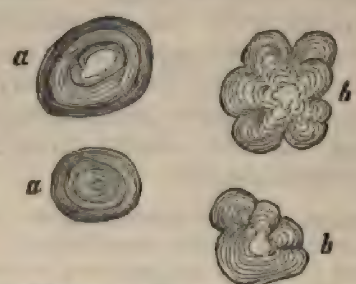


FIG. 134. CHALKY CONCRETIONS.
a, from an inflamed omentum. b, from a tuberculous lymphatic gland.

partially transformed into pale denucleated lumps, which speedily disintegrate.

Such patches may go on to gangrenous putrefaction; or losing fluid may become condensed and cheesy-looking. In the latter case calcification often follows, and the entire gland may be transformed into a chalky or mortar-like mass.

Stratified concretions (Fig. 134 *b*) not infrequently take the place of diffuse calcareous deposits. They are especially common in connection with tuberculous disease.

Degenerations
atrophy
Amyloid
Fatty degeneration
~~Caseation~~
~~Suppuration~~
Necrosis
Calcification
Fibrous induration
inflam

CHAPTER XXVII.

FOREIGN SUBSTANCES IN THE LYMPHATIC GLANDS.

334. Minutely divided **foreign substances** which have gained access to the lymphatic vessels are intercepted and retained for a longer or shorter time in the glands. Thus after hæmorrhage into the tissues the red corpuscles or their remains are conveyed to the glands, and deposited there within the carrier-cells.

At first these carrier-cells with the corpuscles or pigment (hydrated ferrous oxide, Art. 268) they contain are met with mainly in the sinuses (Fig. 135); but afterwards they enter the follicles. Occasionally the deposit may be so large that the proper structure of the gland is obscured by it. The appearance of the gland is altered greatly, and it may be stained dark brownish-red or russet, so as occasionally to recall the look of the spleen-pulp, especially when the coloring-matter of the blood in solution passes into its substance as well as the insoluble pigment.

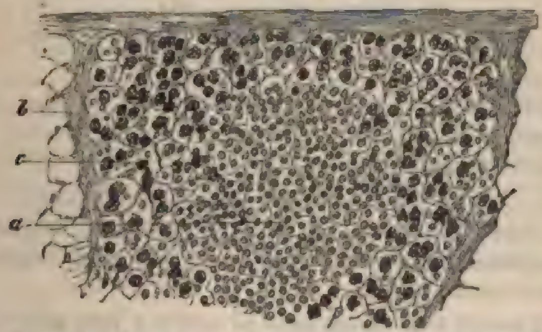


FIG. 135. SECTION OF A LYMPHATIC GLAND CONTAINING PIGMENT-GRANULE CELLS.
(*Carmine staining*: $\times$ 80.)
a, follicle. *b*, trabeculæ. *c*, pigment-granule cells.

Other substances may in like manner be retained in the glands, and if they have any proper color the gland of course becomes pigmented. The most familiar instance is the gray or black pigmentation of the bronchial glands by matters inhaled with the air as dust. When blue or red colors have been used in tattooing the skin, the glands which receive the corresponding lymphatics are often found after a time to contain some of the insoluble pigment.

See VIRCHOW (*Cellular-pathologie* 4th ed. p. 224, *Virch. Arch.* vol. 35), BILLROTH (*Beiträge z. path. Hist.* (1858) p. 135, *Virch. Arch.* vol. 21), REBSAMEN (*Virch. Arch.* vol. 24), ORTH (*Virch. Arch.* vol. 61), HINDENLANG (*Virch. Arch.* vol. 79), SOYKA (*Prag. med. Woch.* 1878), VON INS (*Arch. f. exp. Path.* v.) KELSCH (*Arch. de physiol.* 1875).

335. The **consequences of foreign deposit** in the glands depend on its amount and on its physico-chemical nature. Many substances, such as calcium carbonate, are dissolved; others like coal-dust, stone-dust, or cinnabar remain and lead to permanent pigmentation. They lie enclosed in lymphoid cells (Fig. 136 *c*), or lodged in the reticulum and trabeculæ. If the amount present is small the changes induced are

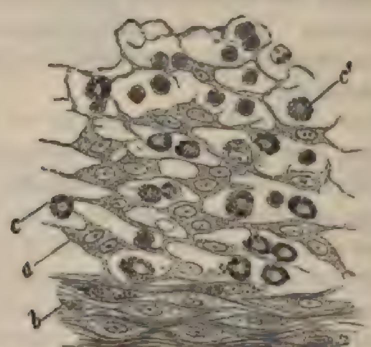


FIG. 136. SECTION OF A SLATE-COLORED BRONCHIAL GLAND.
(*Carmine staining*: × 250.)
a, reticulum of large cells. *b*, fibrillated connective tissue. *c c'*, pigment-carrying cells.

trifling; larger amounts lead to the shrinking of the gland. The lymphoid elements dwindle and disappear, while the meshes of the reticulum become filled with pigment-carrying cells (Fig. 136 *c* and *c'*) and free pigment. The reticulum may be unaltered, or in part hyperplastic (*a*), in which case it is made up of juicy branching and anastomosing cells. Dense fibrillated connective tissue (*b*) is often formed in places, and this too contains pigment.

Chemically active substances have of course a very different effect, as also such living micro-organisms as may reach the glands. They usually set up more or less violent inflammation, and not infrequently lead to necrosis.

CHAPTER XXVIII.

INFLAMMATIONS OF LYMPHATIC GLANDS.

336. **Acute lymphadenitis.** Acute inflammation of the lymphatic glands is usually set up by irritants brought to them by the lymph. In many cases the irritant can be proved to be bacterial, in other instances its nature cannot be ascertained. An inflamed gland is swollen, and often greatly swollen. On section it appears red, and moister and softer than usual, and it often contains hæmorrhagic patches. The abnormal redness may be confined to the cortex, or extend also to the medulla. During the later stages the redness decreases again; and the section becomes mottled, or uniformly grayish, yellowish, or white. The condition of the tissue varies with these changes of tint. Where it is red, the blood-vessels are dilated and distended with blood; the reticulum both without and within the follicles being likewise distended with cells and liquid, while red corpuscles are often found lying free in the parenchyma. Where the tissue is pale, the accumulation of colorless cells has gone on, while the hyperæmia has diminished. The reticulum is seldom notably altered at first, but as the inflammation proceeds it usually breaks down here and there. The number of glands affected by the same inflammation varies much; sometimes a single one, sometimes an entire group, is attacked.

It is difficult to determine with certainty the source of the leucocytes which gather in the reticulum of an inflamed lymphatic gland. The lymphoid cells of the follicles normally multiply by subdivision, and it is possible that in inflammatory conditions the multiplication may be increased. But we cannot exclude the possibility that part at least of the intruding leucocytes are derived from the lymphatics or blood-vessels.

337. The further stages and **terminations** of the acute inflammation are different in different cases. It may end in resolution and complete restoration, or in necrosis, gangrene, caseation, suppuration, or fibrous induration. But before reaching such terminations certain changes pass over the lymphoid elements. Many become fatty and break up into mere lumps of detritus; others undergo coagulative necrosis and change into pale turbid denucleated masses, or into granular flakes of fibrin. Others again are enlarged as if by dropsical swelling; or take on the appearance of formative or fibroblastic cells, being large and granular and having bright vesicular nuclei containing nucleoli.

Then there are large cells containing within them other lymphoid cells or red corpuscles or fragments of these, and incorrectly called 'brood-cells.' Lastly there are numbers of pus-corpuscles, with their nuclei broken into two or more fragments. These changes, only recognizable with the aid of the microscope, are variously combined in different cases; they are followed by the more obvious transformations.

When **resolution** occurs the altered leucocytes are re-absorbed and disappear. The gland becomes flaccid, and again appears hyperæmic; it then gradually resumes its normal condition. In **suppuration** patches of yellowish-white softening appear, and the tissue within them breaks down and liquefies. Not infrequently the entire gland breaks down in like manner forming what is called a **suppurating bubo,** and the inflammatory process then attacks the neighboring tissues. If the gland is near the surface of the skin redness and swelling are observed over the site of the bubo. The suppurating gland may then break into the surrounding tissue, or outwardly if it be superficial. In other instances the pus is partly absorbed, and the rest becomes condensed into a caseous mass. In both cases plastic inflammation is induced round the seat of suppuration; and fibrous tissue is developed round the remaining portions of the gland, if there be any, thus leading to induration; or round the caseous residue, which is thereby encapsuled. When the gland becomes **necrosed,** parts or the whole of the gland die outright, take on a dull gray tint, and become very friable or 'rotten.' If **putrefaction** follows, the tissue becomes dirty, foul-smelling, and semi-liquid. When the tissue was before highly hyperæmic or saturated with extravasated blood, the color of the necrosed gland may be slaty or even black. Necrotic and putrefactive processes of this kind of course set up inflammatory and destructive change in the surrounding tissues. The obliteration and **induration** of the gland require longer time. They are the result of defective reproduction of the lymphoid elements and excessive production and substitution of fibrous tissue, and properly come under the head of chronic inflammation (Arts. 338–341). **Caseation** likewise belongs strictly to the domain of the chronic inflammatory processes.

338. **Chronic lymphadenitis.** The chronic inflammations of lymphatic glands are in general accompanied by increase of their bulk, due to the formation in them of new cellular tissue. This tissue is generally very unstable and reaches only the lowest stage of organization; it is indeed scarcely correct to describe it as tissue at all. Less often it becomes more fully developed, and then it is more permanent in its character. Its structure usually bears little resemblance to that of normal lymphoid tissue, and often is so like neoplastic or tumor tissue that it is difficult for the histologist to be sure whether an enlarged lymphatic gland is really a tumor or merely a hyperplasia. The diagnosis in such cases depends much more on the clinical facts than on the structural appearances.

The tumor-like enlargements of the glands met with in chronic lymph-

adenitis are divisible into four groups according to their histological structure: (1) small-celled hyperplasia with a tendency to caseation or suppuration, commonly described as scrofulous lymphadenitis; (2) large-celled indurative hyperplasia; (3) trabecular or reticular indurative hyperplasia; (4) tuberculous enlargement.

Clinically all these varieties are referred to as **lymphoma.**

339. **Scrofulous lymphadenitis,** or small-celled hyperplasia of the lymphatic glands, is closely related to ordinary acute lymphadenitis and is in fact often a terminal stage of an acute inflammation, though it generally runs throughout a subacute or chronic course. The glands swell to a considerable size. Sometimes a single one is affected, sometimes an entire group such as the cervical or mesenteric glands.

At first the glands are soft and grayish on section; then caseous foci develop, or the whole gland is changed into an opaque white cheesy mass, which may be dry or pulpy or creamy according to the amount of water present. The tissue surrounding the caseous foci is in the early stages soft and grayish, consisting of lymphadenoid tissue infiltrated with inflammatory products; afterwards though still cellular it appears denser and firmer and contains a considerable amount of fibrous tissue. The capsule of the gland is especially liable to be thickened.

In the early stages the chief microscopic change which appears is the great accumulation of small leucocytes in the meshes of the adenoid reticulum. Few larger cells are visible, though cases differ in this respect. Sometimes a number of epithelioid cells are developed, and are aggregated in clusters; and now and then giant-cells appear. The reticulum itself seems little altered at first; but later on it breaks down here and there. When necrosis or caseation sets in the usual degenerative metamorphoses are visible; the cellular tissue is replaced by a mass of detritus, and only the nuclei at the margins where the dead tissue passes into the living can be brought out by staining reagents. In recent specimens this marginal zone is seen to contain numbers of fatty cells and pale coagulated masses. Occasionally the necrotic disintegration is preceded over a greater or less extent by uniform homogeneous degeneration.

340. **Large-celled indurative hyperplasia** of the lymphatic glands is distinguished by the transformation of the normal gland-tissue into a large-celled tissue having none of the characters of the original structure. The large-celled tissue consists in part of close-packed rounded or polygonal cells (Fig. 137 *b*), and in part of spindle-cells. There is but little intercellular substance, though in some spots distinct patches of fibrous tissue are seen. If the proper lymphadenoid tissue has not entirely disappeared, the remaining portions of it form reticulated bands (*a*) pervading the large-celled tissue. The latter stains less deeply than the small cells of the normal lymphadenoid tissue.

The process of transformation begins with an accumulation of leucocytes in the gland-tissue, followed by the development of epithelioid cells

[illegible] at first, and [illegible] though they are [illegible] large cells can [illegible] reagents. The [illegible] ones, though [illegible] made up of [illegible] a diffuse [illegible] The latter very [illegible] is occasionally [illegible] (Art. [illegible]

[illegible] firm and dense [illegible] small hen's egg. Th[illegible] translucent; after expo-

FIG. [illegible]. [illegible]

[illegible]

a [illegible] b [illegible]

c [illegible]

to the air it becomes brownish. Little fluid can be obtained from it by scraping. In the nodular form of the affection the nodules stand out from the surrounding tissue by virtue of their tint and translucency. Soft caseation does not usually follow upon large-celled hyperplasia, but homogeneous or hyaline degeneration is common; it leads to the entire destruction of the cells, and must be reckoned as a form of firm caseation (Art. 97). The tissue becomes homogeneous and shining and loses its nuclei, or seems broken up into hyaline denucleated blocks. Now and again this stage passes into one of complete disintegration with granular crumbling of the tissue, not unlike soft caseation.

341. **Fibrous indurative hyperplasia.** Hyperplasia of the adenoid reticulum has already been referred to (Art. 335) in speaking of the consequences of long continued deposition of foreign substances in the glands. The increase of fibrous tissue in such cases is however but slight, when

compared with the very notable fibrous hyperplasia which may result from chronic or often-repeated inflammation, and which may lead not merely to induration but to great increase in the size of the gland. The swellings thus produced may reach the size of a hen's egg, or more.

The capsule and fibrous septa are in general the parts most thickened and enlarged, or at least the more diffuse hyperplasia starts with them. The hyperplasia being thus due to the formation of new fibrous tissue, the affection is best described as a fibrous hyperplasia (or '**elephantiasis**') of the gland, and we may distinguish the **trabecular** or interstitial from the diffuse or **reticular** variety. The most typical examples are found in cases of elephantiasis of the skin and subcutaneous tissue. When the change has originated in the capsule or septa, the section of the gland is seen to be surrounded by a broad zone of fibrous tissue, and the grayish parenchyma is pervaded by lustrous white fibrous bands.

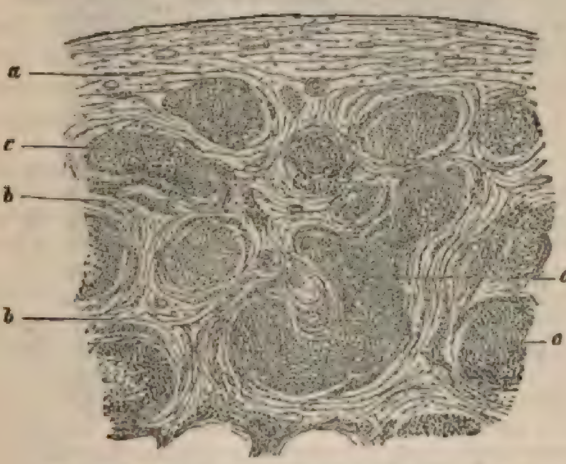


FIG. 138. FIBROUS HYPERPLASIA OF A LYMPHATIC GLAND.
(*Hæmatoxylin staining:* ×25.)
a, thickened capsule. b, fibrous bands pervading the gland.
c, isolated remnants of gland-tissue.

pressed by glands the fibrous framework is always greatly increased in proportion to the rest of the tissue; the fibrous septa and sheaths of the vessels become thick fibrous cords (Fig. 138 *b*), and the essential parenchyma is reduced to isolated patches (*c*) scattered through the gland, and compressed by the fibrous overgrowth.

When the hyperplasia is more generally diffused, the gland on section has a uniform light-gray tint and is uniformly dense and firm.

342. **Tuberculous lymphadenitis** is a very common and a very noteworthy affection. The tuberculous bacillus usually reaches the glands by way of the lymphatics; and as it sets up tuberculous disease at its point of entrance into the body, the affection of the glands is what we

CHAPTER XXIX.

TUMORS OF LYMPHATIC GLANDS.

343. The non-inflammatory tumors of the lymphatic glands fall into two main groups, according to their histological structure. The first group includes all growths whose general type is that of normal lymphadenoid tissue; the second includes those in which the normal tissue is displaced by tissue of a different kind. The tumors of the first group are variously known as lymphomata, lymphadenomata or adenomata simply, and lymphosarcomata; those of the second group are chiefly sarcomata. The former are homœoplastic, the second heteroplastic growths (Art. 138). It is not always easy to determine whether a given glandular growth, homœoplastic or heteroplastic, is to be reckoned as a true tur in the stricter sense of the term. Many of the homœoplastic formati have the anatomical characters of hyperplasia, rather than of neopla And these characters are to some extent borne out by the fact that function of the gland often becomes more active as its growth increa that is to say a larger number of white corpuscles are contributed by it the blood (**leukæmic lymphoma**). On the other hand there are ca in which glandular growths of like structure exhibit the clinical char ters of tumors, that is to say they form metastases and induce cache (**malignant lymphoma**); and the cachexia—taking the form of emac tion, dropsy, coma, delirium, etc.—may result in death.

Owing to the difficulty of distinguishing neoplasm from hyperplas we shall in what follows describe all the glandular growths under t general head of tumors, classifying them according to their structure.

It is highly probable that closer investigation of the development of the gl dular tumors will make it possible to distinguish the various forms more ac rately than we are at present able to do. We are now unable to give a explanation of the fact that of two cases of lymphoma which are histologica identical, one should involve alteration in the blood, and the other should n And we know as little the reason why one lymphoma should continue to be purely local affection, and another of the same texture should lead to metasta infection of other groups of glands or of organs which normally contain no gland-tissue.

KLEBS has suggested that leukæmic lymphoma may be an infective disorder due to an extraneous virus, and he has therefore classed it with the infective granulomata. This view has much in its favor, but we are at present unable to advance any definite proofs of its correctness.

References:—Art. 328; VIRCHOW, *Kran* *Geschwülste* II.; WUNDERLICH,

Arch. d. Heilk. VII.; MURCHISON, *Path. Soc. Trans.* 1870; LANGHANS, *Virch. Arch.* vol. 54; POTAIN, *Dict. encyc. d. sciences méd.* (2d ser. 1870) vol. III.; HUMBERT, *Des néoplasmes des gang. lymphatiques* Paris 1878; VON WINIWARTER, *Arch. f. klin. Chir.* XVIII.

344. **Soft lymphadenoma** or lymphosarcoma is a soft almost fluctuating or diffluent growth, with a light-gray or grayish-white or grayish-red tint on section. It is sometimes speckled with small red islets corresponding to dilated vessels or small extravasations. An abundant turbid juice comes from the section when scraped. The tissue surrounding the gland is not usually altered, though sometimes neighboring glands cohere and coalesce into a single mass. Sometimes caseous patches occur within the growth. The juice consists of small leucocytes, mingled with a few larger and often multinuclear cells, spindle-cells from the walls of the vessels, red corpuscles, and free nuclei.

When examined with the microscope the follicles are seen to be greatly enlarged, the fibrous parts of the medullary tissue have disappeared, and the whole section of the gland has become like the cortex. In pencilled sections the reticulum is seen to be thickened; it has nuclei at its nodal points, and includes a multitude of lymphoid elements. The growth is thus due to a development of tissue similar to that of the normal gland-follicles.

The affection extends in some cases only to one or two glands, in others to whole groups. Other parts of the lymphatic system are very often affected at the same time, especially the malpighian follicles of the spleen and the lymphadenoid tissue of the alimentary canal, as it exists for example in the follicles of the tongue, the stomach, and the intestine. In young patients the thymus may likewise be affected. But lymphadenoma may also develop in parts which normally contain no lymphadenoid tissue, such as the bones, liver, kidneys, ovaries, etc.

The behavior of the blood varies, and two varieties of the disease are distinguished accordingly. In many cases no change can be detected, or only a diminution in the amount of blood. This variety is called by various names such as **Hodgkin's disease** (from its first describer), adenia (TROUSSEAU), lymphosarcoma in a restricted sense (VIRCHOW), malignant lymphoma (BILLROTH), and pseudoleukæmia (COHNHEIM). In the second variety the white corpuscles of the blood are increased in number (leukæmia). The growth is then described as **leukæmic lymphoma** or leukæmic lymphadenoma. The examination of the blood suffices to distinguish the varieties; in other respects the affections are identical. (On the changes in the blood see Art. 260; on those in the spleen see Art. 328.)

The leukæmic increase of the white blood-cells very often leads to considerable deposits of them in the various tissues. The deposits may be diffuse or in agglomerated masses, and must not be confounded with the lymphadenoid growths.

LANGHANS (*Virch. Arch.* vol. 54) has proposed to call both varieties by the one name of **adenia**, distinguishing them as simple adenia and leukæmic adenia. Some such distinction would be better than the present confusion. We do not know the ultimate cause of the difference between the two varieties; cases are known in which the simple form has passed into the leukæmic, and inversely.

The spleen is affected in both forms. In simple or non-leukæmic cases it is sometimes firm, sometimes soft, the follicles are enlarged to the size of a hazel-nut, and are grayish-yellow, vascular, and ecchymosed. It is rare for the spleen to be more intensely affected than the glands; while in leukæmic adenia the affection of the spleen is often the most marked feature of all.

References:—Arts. 260 and 328; CORNIL, *Arch. gén.* II. (1865) p. 207; COHNHEIM, *Virch. Arch.* vol. 33; HODGKIN, *Med. chir. Trans.* XVII. (1832); EBERTH, *Virch. Arch.* vol. 49; B. SCHULZ, *Arch. d. Heilk.* 1874.

345. **Hard lymphadenoma** or lymphosarcoma occurs as a primary growth most frequently in the superficial lymphatic glands; other groups may be attacked in the further course of the affection. For example, if the affection start in some of the cervical glands, the rest of the cervical glands, and the thoracic and abdominal glands lying near the large vessels, are attacked in succession. The glands are transformed into firm tough elastic or hardened knots, forming dense clusters in combination. Single glands may reach the size of a walnut.

The section of such a knot becomes very slightly concave, and but little juice runs from it; it looks pale yellowish-white, and may be translucent or opaque; sometimes small hæmorrhages appear in it. The capsule and surrounding tissue seldom exhibit any great degree of fibrous thickening.

On microscopic examination the lymphadenoid structure is seen to be preserved (LANGHANS), while the cells are increased in number and the reticulum is thickened. The cells resemble the ordinary lymphoid elements, a few being larger or multinuclear. The strands of the reticulum are broad and fibrillated, and they seem multiplied so that the network is closer and its meshes smaller than in a normal gland. The follicles and sinuses are no longer distinguishable. The adventitia of the vessels is thickened and is made up of shining fibrous bundles. Fatty degeneration, calcification, or softening rarely supervene. In later stages the follicles of the spleen may be affected, and be changed like the glands into hard nodules. The spleen is never primarily affected in this form of lymphadenoma. Similar nodules may be developed in the lymphadenoid tissue of the alimentary canal and in the thymus. Metastatic growths occasionally appear in the liver, kidneys, lungs, etc. Leukæmia does not accompany this affection.

Certain transitional varieties between hard and soft lymphadenoma have been described.

346. **Sarcoma** of the lymphatic glands is a somewhat uncommon affection. It occurs in single glands, or several of the same group are simultaneously affected and cohere into a nodular tumor. It often over-

passes the limits of the gland and invades the adjoining tissues. Secondary growths are usually developed. Small-round-celled sarcoma, spindle-celled sarcoma, fibro-sarcoma, and alveolar sarcoma or alveolar angiosarcoma, are all forms which occur. The latter form has a somewhat carcinoma-like structure, the epithelioid cells being grouped in clusters within an alveolar stroma.

It appears that the neoplasm may start in various parts of the gland-tissue. According to PUTIATA alveolar sarcoma begins in the tissue around the vessels. In other instances, especially in spindle-celled sarcoma, the connective-tissue framework is the primary seat of neoplastic proliferation (WINIWARTER). Some authors, like PUTIATA, maintain that the lymphoid elements may be transformed into tumor-cells.

See LANGENBECK (*Deutsche Klinik* 47. 1860), BILLROTH (*Beiträge z. path. Hist.* Berlin 1858), PUTIATA (*Ueb. Sarcom. der Lymphdrüsen, Virch. Arch.* vol. 69), VON WINIWARTER (*Arch. f. klin. Chir.* XVIII.), VAILLARD (*Revue de méd.* 1882).

347. **Secondary growths.** All the forms of tumor which give rise to metastases may affect the lymphatic glands. Cancers especially are apt to do so, and the glands become enlarged and altered as the disease advances. On section they have a white marrowy look, and cancer-juice can be obtained from them by scraping. The altered glands have not always the same appearance, any more than the primary tumor from which they are derived. Indeed the typical structure of the parent tumor is often very beautifully reproduced in the infected gland. The secondary growths likewise pass through the same series of changes as the parent tumor (Art. 174).

The gland-tissue is compressed and displaced by the cancerous growth. The cancer-germs brought to the gland in the first instance by the lymphatics begin to germinate in the sinuses. Cancer-nests are then formed, and the stroma of the tumor is developed out of the lymphadenoid tissue. In its first stages the cancerous change is often not apparent to the naked eye, and must be searched for with the microscope. Sometimes even the more advanced changes are not to be made out in fresh specimens without minute examination.

Sarcomatous metastases, like the carcinomatous, may originate in sarcoma-cells which have entered the gland through the lymphatic vessels.

SECTION IV.

THE SEROUS MEMBRANES.

CHAPTER XXX.

DEVELOPMENT OF THE SEROUS CAVITIES.

348. The **primitive body-cavity** is a large undivided space interposed between the alimentary tract and the body-wall, and shut off in all directions from the blood-vessels (HERTWIGS). Until recently it was held that the body-cavity was directly connected with the vascular system; HAECKEL indeed taught that it was originally in itself the first rudiment of a vascular system. But embryological research has now shown that this view is untenable. The blood-vessels and lymphatics arise independently of the body-cavity as excavations in the substance of the mesoblast, due to partial liquefaction of the tissue and the transformation of some of the cells into blood-corpuscles. The body-cavity on the other hand is originally a part of the primitive alimentary cavity or archenteron. Two lateral diverticula of this are formed and gradually abstricted from the central cavity which persists as the ultimate alimentary tract. These diverticula then converge ventrally and coalesce to form one cavity, the ultimate body-cavity; and this surrounds the alimentary tract except dorsally, where the primitive dorsal septum between the diverticula persists as the mesentery. The connection ultimately existing between the lymphatic system and the body-cavity are later and secondary developments (HERTWIGS and BALFOUR).

The mode of origin of the body-cavity indicates the true nature of its lining membrane. The cavity not being a mere lymph-space, like the sac of the arachnoid, is clothed not with endothelium but with an **epithelium** derived originally from the hypoblast. Under this single layer of epithelium lies a layer of connective tissue richly provided with blood-vessels and lymphatics, which latter communicate freely with the body-cavity through a multitude of ostia or **stomata**. The membrane formed by the layer of cells and the layer of connective tissue is known as a **serous membrane**; and, after the differentiation of the general body-cavity, as peritoneum, pleura, or pericardium, as the case may be.

This account of the origin of the vertebrate body-cavity has a pathological as well as an embryological bearing. If the cavity is not a mere lymph-space, its pathology is not strictly comparable with that of the lymphatic system. If its epithelial covering is originally derived from the alimentary or splanchnic epithelium its morbid changes will be related to those of the mucous membranes, and must be studied in con-

nection with them. Thus, for example, it may be important in discussing the genesis of neoplasms occurring in a serous membrane to bear in mind that its so-called endothelium is genetically a true epithelium.

Few affections of the serous membranes are independent or confined to them alone. Various organs are enclosed within the body-cavities and are thus in the closest relation to the serous membrane. The disorders affecting the membrane are consequently in the greater number of cases secondary to affections of the organs which it covers. These secondary affections will be discussed in treating of the respective organs; in the following chapters we shall deal chiefly with the primary or independent affections of the serous membranes.

The above account of the origin of the body-cavity differs essentially from that given in the first German edition, in which the widely-accepted view which regards the pleuro-peritoneal cavity as a mere lymph-space was adopted. The works of the HERTWIGS (*Die Coelomtheorie* Jena 1881) and BALFOUR (*Comparative Embroyology* vol. II. ch. 13) have shed new light upon the subject; and though they differ in details the main fact of the derivation of the body-cavity from the primitive alimentary cavity seems established by them.

The fact that the serous membranes are capable of performing secretory functions seems to harmonize with the theory that they are originally derived from the secretory layer of the blastoderm, the hypoblast.

CHAPTER XXXI.

EFFECTS DUE TO DISORDERS OF THE CIRCULATION.

349. Disorders of the circulation affecting the serous membranes are very common.

Congestive hyperæmia such as accompanies the early stages of inflammation, and sudden diminution of the normal pressure within the serous cavity, may lead to intense reddening of the surface of the membrane. In passive hyperæmia it is the veins especially which are engorged, and often notably dilated.

Small circumscribed **hæmorrhages** are very commonly met with, both in inflammation and in fatal cases of infective disease, renal and cardiac disease, asphyxia, etc. When fresh they are red, but after a time they become brown or slate-colored. They are due either to alterations in the vessel-walls, or to extreme vascular engorgement with obstruction, or to both together.

Large hæmorrhages, in which blood escapes in quantity into the cavity, may result from very various causes. They are frequently due to mechanical injury by which a large vessel is opened, as in ruptures of the liver, kidney, spleen, lung, etc. Such are also the grave hæmorrhages that follow rupture of the heart or aorta or other artery depending on disease, and rupture of the fœtal sac in tubal pregnancy. Sometimes no lesion can be made out, as in cases of hæmorrhagic diathesis. New-formed vessels in inflammatory tissue are especially apt to give way and bleed. Lastly, extreme engorgement such as ensues on thrombosis of the portal vein, or embolic occlusion of an artery, may cause very severe hæmorrhage.

The blood poured out into the serous cavity is quicky absorbed by the lymphatics which communicate with the cavity, unless special morbid alterations of the membrane stand in the way. Blood which remains liquid is very speedily taken up, in part without much alteration, and in part after solution or decolorization of the red corpuscles. Coagula are less manageable, but they too are ultimately absorbed. Extravasations in the membrane itself or in the subserous tissue are dealt with in the manner described in Arts. 112–116. As the blood disintegrates, either before or after its complete absorption, urobilinuria or hæmoglobinuria is observed.

VON RECKLINGHAUSEN (*Virch. Arch.* vol. 26) was the first to investigate with success the process of absorption of foreign substances (such as milk, tinted liquids, and blood) in the abdominal cavity. PONFICK (*Virch. Arch.* vol. 48) and CORDUA (*Ueber d. Resorp. von Blutergüssen* Berlin 1877) have made out certain further details. They injected fibrinous or defibrinated blood into the abdominal cavity, and found that the defibrinated blood was very rapidly taken up, and that almost without alteration. This observation has a practical value, for it suggests the possibility in the human subject of successful transfusion of defibrinated blood into the abdomen instead of into a blood-vessel. The blood-cells so absorbed survive when they reach the circulating blood.

Unchanged blood when injected into the abdominal cavity is much less readily absorbed, as clots form which become aggregated into considerable masses. These by their close contact with the serous membrane set up inflammation, are fixed down by exudations, and receive a covering of migratory cells. Large formative cells with an abundant protoplasm then appear on the surface of the clot. They are developed from the white blood-cells, and presently lead to the formation of new fibrous tissue, while new vessels are produced by off-shoots from the vessels of the serous membrane. Meanwhile the inner parts of the clot are disintegrating and dissolving. The red corpuscles are changed to grains of pigment or are taken up by carrier-cells (Art. 68), or give up their coloring matter which is deposited in the form of blood-crystals, while the albuminous detritus is absorbed.

Other matters capable of absorption, such as recent dead tissue, and to some extent tissue hardened in alcohol, are dealt with in like manner. Bodies that cannot be absorbed are usually overlaid with fibrous tissue and so fixed down. If they are altogether insoluble and non-irritating (like glass) they may remain for long in the cavity without setting up any inflammation.

350. Large accumulations of serous fluid in the body-cavities are very frequent. The accumulation is described as **ascites**, **hydropericardium**, or **hydrothorax**, according as it occurs in the abdominal, pericardial, or pleural cavity. The fluid is colorless or pale yellow, clear or opalescent, and sometimes after death it is found to be turbid from the presence of shed epithelium. Sometimes too it contains a few delicate shreds of fibrin. If jaundice is present, the fluid may be bile-stained; if hæmorrhage has occurred it may be blood-stained. If any solution of continuity has occurred in the larger lymphatic vessels of the abdomen, the ascitic fluid may be rendered white and milky-looking by the chyle which escapes (chylous ascites).

The effused fluid is poor in formed elements. Occasionally flakes of shed epithelium are found, in the form of large nucleated granular cells, containing fat-globules or otherwise disintegrating. Lymphoid cells are scanty. Hæmorrhagic effusions contain blood-cells; chylous effusions contain lymphoid cells and fine granules and drops of oil. When a tumor exists in the cavity the effusion may contain tumor-cells, which are usually in a state of fatty or mucoid degeneration. Highly fatty detritus if present in any quantity may give the fluid the look and consistence of whey.

We have already described the conditions under which fluid accumulates in the serous cavities (Arts. 23–25). The main cause of increased

transudation from the vessels is obstruction of the venous outflow, aided by damaged or degenerate conditions of the vessel-walls. Ascites is most commonly due to uncompensated cardiac disease, pulmonary emphysema, or degenerative change in the kidneys. It is also common in liver-disease by which any considerable extent of the portal territory is obstructed, and it often accompanies the development of abdominal tumors. According to QUINCKE (*Deutsch. Arch. f. klin. Med.* XXX.) it may make its appearance in girls about the time of puberty without apparent cause, disappearing as soon as menstruation is established.

The most immediate result of serous effusion is the displacement and compression of the organs it involves. This is very apparent in the case of the lungs, which may be thrust back against the spine by a large pleural effusion. The compression of the heart and abdominal viscera by effusion into their respective serous cavities is less marked, as the pericardium and peritoneum are capable of great distention. But even then serious impairment of the functions of the organs may ensue. Extreme ascites presses up the diaphragm and impedes the breathing; a great pericardial effusion may interfere with the action of the heart, chiefly by impeding the diastolic expansion. If effusion occur simultaneously in the several cavities, the disturbance of the visceral functions may become very grave.

The anatomical changes observable in the serous membranes in dropsical conditions are often very slight. They may be little more than result from the soaking of the serous and subserous tissue; or perhaps the veins may appear more or less dilated. After long-continued dropsy due to engorgement whitish thickenings and fibrous adhesions make their appearance on the surface of the membrane. The former are chiefly due to alterations in the epithelial cells, which are more or less swollen, partially lifted from the fibrous basis-tissue, and in process of desquamation or fatty degeneration. Proliferous cells with an abundant protoplasm and two or more nuclei are also to be met with. The vascular engorgement thus induces catarrh with desquamation and multiplication of the epithelium (Fig. 142). The fibrous tissue is often largely infiltrated with leucocytes, and these may after a time proceed to develop into new fibrous tissue, producing diffuse circumscribed thickenings of the serous membrane, and adhesions of separate parts.

CHAPTER XXXII.

INFLAMMATIONS OF SEROUS MEMBRANES.

351. **Inflammation of the serous membranes** is the most important of the affections to which they are liable. Our knowledge of its nature and general course is now full and complete. We mentioned in Art. 95 that COHNHEIM made his fundamental observations on the process of inflammation by means of experiments on the mesentery of the frog. In the human subject the omentum is very well adapted for microscopical examination, and that even without any special treatment; but

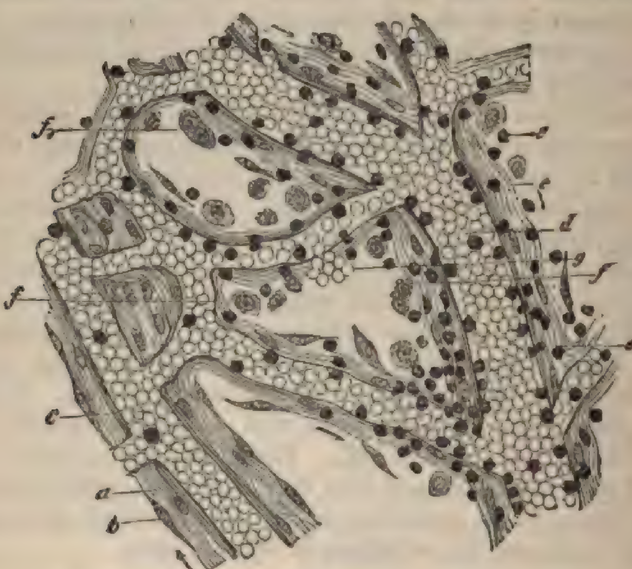


FIG. 140. INFLAMED OMENTUM FROM THE HUMAN SUBJECT (×200).

a, normal fibrous trabecula.
b, normal epithelium.
c, small artery.
d, vein with colorless blood-cells peripherally disposed.
e, colorless blood-cells migrated or migrating.
f, desquamated epithelium commencing to break down.
f_1, multinuclear cell.
g, migrated red blood-cells.

the inflammations of the pericardium and pleura are also easily investigated.

The first stage generally consists in the formation of an exudation

composed of blood-cells (Fig. 140 *e*) and liquid; and this collects in the meshes of the tissue or on its surface, while the epithelium desquamates and disintegrates (*f*). Only when the inflammation is very slight does the epithelium remain intact, or proceed to multiply: when the irritation becomes at all intense and the exudation abundant, the epithelium perishes.

Three chief forms of inflammation are distinguished according to the character of the exudation, namely the fibrinous, the sero-fibrinous, and the purulent. The fibrinous forms are often spoken of as adhesive or plastic, inasmuch as they generally lead to the formation of adhesions and false membranes between the serous surfaces.

352. **Fibrinous and sero-fibrinous** inflammations. In recent fibrinous inflammation the serous membrane is injected, and its surface turbid and dulled. The dullness appears especially when the surface is wiped; and is essentially due to the deposit of a light grayish or yellowish film of fibrin. If the deposit be at all thick, it may conceal the redness of the injection.

The first fibrinous deposits take the form of minute granular or reticulated masses. The epithelium lying between the little masses is often intact, but it may begin to be shed. In the more intense inflammations the epithelium may be changed into a homogeneous or granular and generally denucleated membrane, that is to say it undergoes coagulative necrosis. Such fibrinous deposits may be unaccompanied by any large amount of liquid exudation. What there is present is rendered turbid by shed epithelium and migrated leucocytes. An inflammation of this kind is often referred to as a '**dry**' inflammation (dry pleurisy, pericarditis, or peritonitis). It frequently results in adhesions of the serous surfaces.

When the exudation is more abundant, liquid is poured out and accumulates in the cavities. The pericardium or pleura becomes notably distended at the expense of the lungs. In the abdomen the liquid gathers first in the dependent parts; but as the effusion increases the organs may be compressed, and the abdominal wall greatly distended.

The proportion of cells and fibrin in the effusion varies greatly. When cells are abundant, the liquid is highly turbid; if red corpuscles have escaped from the vessels the liquid will be more or less reddened, and petechiæ may be observed on the surface of the serous membrane (**hæmorrhagic** inflammation). The fibrin forms threads and curdy flakes, which are translucent and yellowish, or opaque and whitish, according to the proportion of leucocytes they enclose. When very abundant the fibrin is precipitated on the surface of the inflamed membrane and forms a thick adherent layer. The surface of the layer is usually rough and occasionally even villous in appearance, as in the case of the heart (*cor villosum*), or it may take the form of reticulated or lattice-like prominences recalling the look of the reticular stomach of a ruminant.

When the amount of liquid effused is small and the fibrin abundant, thick **false membranes** are formed between the visceral and parietal layers of the serous membrane.

The extent of the inflammation varies much in different cases. In one case only a single patch of the pericardium may be inflamed, and in another the whole surface of a lung.

When the exudation has reached a certain point the inflammatory process ceases and, unless new irritation sets up new inflammation, the process of repair begins. This primarily consists in the **absorption** of the effusion; but it is generally associated with the formation of new fibrous tissue.

The liquid portions are of course the most easily absorbed; but the quickness with which this is effected is not always the same. If the blood-vessels and lymphatics readily resume their functions, the lymphatic channels and stomata being again opened up, the effusion may very speedily disappear. If the mouths of the lymphatics remain closed, the absorption may be very slow indeed.

Fibrin is less readily absorbed; but it is ultimately made more easy of absorption by disintegration and solution. Now and again residues remain unabsorbed, and these usually become calcified. The presence of fibrinous masses which act as dead or foreign bodies and set up renewed inflammation may bring about the development of inflammatory fibrous tissue. From four to six days after the beginning of a fibrinous pleurisy or pericarditis small new-formed vessels can be seen passing from the connective tissue of the serous membrane into the fibrinous masses which overlie it; they are made very apparent if the fibrinous covering is gently peeled off. This is a sign that tissue-formation has begun. In the deeper layers of the fibrinous membrane (Fig. 141) formative cells (*f*) can already be seen, and these are the builders of the future fibrous tissue.

The epicardial tissue (*a*) is beset with a multitude of leucocytes (*d*), the blood-vessels (*c*) are crammed with blood, the lymphatics (*e*) with cells and granular coagula. Leucocytes are aggregated in the meshes of the fibrinous membrane, and from them are developing formative cells (*f*), distinguished by their large transparent vesicular nuclei and their granular protoplasm. They are of various shapes, and form connections with the epicardial tissue and with each other. Fibrous tissue is ultimately developed from their protoplasm, and new vessels very soon arise between them as off-shoots from the epicardial vessels. As the fibrous tissue is gradually elaborated the fibrin disappears.

The consequences of the growth of the new tissue are various. If the amount of it is small, it may simply give rise to a slight thickening of the serous membrane taking the form of a more or less sharply defined lustrous white spot, spoken of as a callosity or **milk-spot.** If the new tissue is more abundant, it may take the form of thick almost cartilagin-

ous *plaques* or patches, or of diffused tendinous or scar-like thickenings.

353. **Plastic pericarditis.** Plastic inflammation of the pericardium is usually an independent affection, but it may be associated with endocarditis and myocarditis, or be the result of pleuritic or mediastinal inflammation.

Slight and localized pericarditis very often gives rise to the formation of the milk-spots just referred to; they may occur in considerable numbers and vary from a few millimetres to some centimetres in diameter. Sometimes the greater part or the whole of the pericardium may be covered with similar white thickenings.

The heart itself may be either free, or involved in adhesions; and these latter may consist of a few thread-like bands stretching from the visceral to the parietal layers, or they may extend over the entire surface, binding the heart everywhere to the parietal layer (*concretio pericardii*). Sometimes the adhesions are brittle and easily broken down; in other

FIG. 141. ADHESIVE PERICARDITIS.

(*Section through the pericardium and overlying false membrane*: × 150.)

a, epicardial or visceral pericardium.
b, fibrinous false membrane.
c, distended blood-vessel.
d, leucocytes infiltrating the tissues.
e, lymphatic filled with cells and small granular coagula.
f, formative cells within the false membrane, derived from migrated leucocytes.

cases they are not to be separated without tearing the heart-wall. If the exudation has been highly fibrinous, fragments of unabsorbed fibrin may lie for long between the two surfaces, and may ultimately become calcified. A like change occasionally involves the new tissue itself, and thus the heart may come to be surrounded with a carapace of calcareous plates. Pericardial adhesions are a common cause of cardiac hypertrophy (Art. 279).

Plastic pleurisy occurs as an independent affection, and also as an accompaniment of various pulmonary inflammations. Slight attacks give rise to a moderate amount of pleural thickening, and to the forma-

tion of delicate adhesions. After long-continued or often-repeated inflammation very dense and extensive false membranes may be formed, and the resulting adhesions may be extremely firm and tough (see the Chapters on pulmonary affections). The absorption of the effusion is often slow, especially when it becomes condensed to a cheesy consistence. In this case it may become calcified, as may also the new-formed fibrous tissue in the adhesions.

Plastic peritonitis likewise occurs independently, and also as a secondary result of various inflammatory affections of the abdominal viscera. In the latter case it is usually localized to the neighborhood of the affected organ, such as the liver, spleen, ovary, stomach, etc. Simple thickening of the peritoneum is a less common result; but it does occur, especially in connection with the spleen (see Art. 321). Adhesions are usually formed, and are slight or dense according to the duration of the inflammation. Delicate false membranes are very apt to be the seat of hæmorrhage (hæmorrhagic peritonitis).

In general peritonitis, which is primary and chronic, very considerable thickenings of the membrane may be produced. They may be diffuse or localized, and are sometimes scar-like or even cartilaginous in density. The mesentery when so thickened usually contracts; the omentum may shrink into a kind of roughly-twisted rope (*peritonitis deformans*). The various organs are extensively adherent, the loops of the intestines being sometimes glued into a single mass, while the liver and spleen may be completely enclosed in adhesions. The effused liquid may be scanty or abundant, and the proportions of albumen and of cells it contains vary with the stage and intensity of the inflammation.

The peritoneal inflammation here described occurs chiefly as a result of intense engorgement of the abdominal vessels, such as follows upon valvular disease of the heart or hepatic disease: and it may be accompanied by an abundant dropsical or ascitic effusion.

354. **Purulent inflammation** of the serous membranes is either primary, or developed from an originally sero-fibrinous inflammation by an increase in the inflammatory migration of blood-cells. No sharp line can be drawn between sero-fibrinous and purulent inflammation; for various intermediate or fibrino-purulent varieties occur in which the exudation is pus-like, while at the same time it contains soft white cellular flakes and curds of fibrin. The organs are in such cases covered with a film of purulent fibrin, and may be cemented together by it.

The exudation sometimes becomes putrid, that is to say it becomes discolored and foul-smelling. This is most apt to occur in abdominal inflammation, depending on septic processes in the uterus or its appendages, or on the escape of fæcal matters from the intestine. The putrid exudation contains multitudes of micrococci, single or in chaplets, and occasionally microbacteria.

In all recent inflammations whether fibrino-purulent, purulent, or

putrid, the membrane is intensely injected, its connective tissue infiltrated with leucocytes, and its epithelium destroyed. The pus-corpuscles of the exudation rapidly become fatty and break down. Purulent effusions are much less readily absorbed than serous effusions. Death often intervenes while the inflammation is at its height. In favorable circumstances the absorption may be complete; but usually the liquid parts only are removed, while the fatty disintegrated pus-corpuscles become condensed to a caseous mass which long lies unabsorbed, and may ultimately become calcareous. As the presence of the pus keeps up the inflammatory process granulations and fibrous tissue may at length be developed, producing fibrous bands and adhesions of great extent.

Thus the pleura, where it is in contact with a circumscribed purulent effusion (**empyema**), becomes covered with granulations and in time thickens into a dense tough fibrous membrane. If the pus is absorbed or removed by operation the thickened layers of the pleura grow together into a stout cicatricial adhesion. General purulent peritonitis and purulent pericarditis usually end fatally while the inflammation is still at its height.

CHAPTER XXXIII.

TUBERCULOSIS OF SEROUS MEMBRANES.

355. **Tuberculosis** attacks the serous membranes in three distinct ways. It may be a local manifestation of general miliary tuberculosis; or the tuberculous infection may be conveyed to the serous membrane from some contiguous focus of tubercle in one of the organs; or it may be primary, that is to say no other primary focus of infection may be discoverable.

Three forms may be distinguished according to their anatomical characters. In the first the tubercles appear without inducing any general inflammation; this is chiefly the case in miliary tuberculosis. In the second the eruption of tubercles is accompanied with extensive inflammatory changes and with effusion of liquid. In the third the inflammatory changes come to the front, the tubercles being everywhere as it were embedded in inflamed or new-formed inflammatory tissue. There are however no sharp lines to be drawn between the three forms, which often pass one into the other.

356. The eruption of gray tubercles in general miliary tuberculosis, unaccompanied by diffused inflammation, is most commonly observed in the pleura and peritoneum; it is rare in the pericardium. The gray nodules consist of aggregations of small leucocytes surrounding the small vessels (Art. 123). The epithelial cells may long remain unchanged, but they are ultimately shed and disappear.

Eruptions of miliary tubercles accompanied by moderate inflammatory action are met with chiefly in cases where the serous membrane is infected from a contiguous focus of disease, such as a tuberculous lymphatic gland, a carious vertebra, a phthisical lung, or a tuberculous ulcer of the intestine. Cases occur in which no such starting-point can be made out, and in these we are obliged to consider that the affection is primary in the serous membrane: the peritoneum is by far the commonest seat.

The tuberculous eruption is sometimes local, for instance it may be confined to the true pelvis, to the neighborhood of the spleen, or to a single spot of the pleura or pericardium; or it may extend over an entire membrane or over more than one, as for example over pleura and peritoneum simultaneously. In the latter case there is usually some fluid effusion, and sometimes it is stained with blood. The number of tuber-

cles may be quite small, or so great that the surface of the membrane feels finely granular. The tissue around the tubercles is injected and often beset with minute hæmorrhagic patches *Post mortem* these latter may have a slaty gray look from the formation in them of ferrous sulphide (Art. 68), or they may be brown or black from other alterations in the blood-pigment. If the affection lasts any time the membrane is usually thickened, and the mesentery and omentum become contracted and deformed. Surrounding the tubercles zones of highly-vascular delicate semi-translucent fibrous tissue are often developed.

Corresponding to the obvious appearances just described we always find on examination that the neighboring tissue is more or less exten-

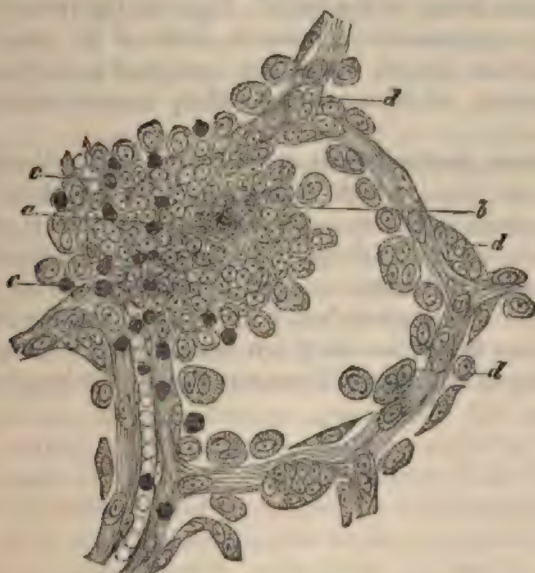


FIG. 142. TUBERCULOSIS OF THE OMENTUM

(*Carmine staining:* × 200.)

a, centre of the tubercle.
b, epithelioid cells.
c, lymphoid cells.
d, proliferous epithelial cells in the neighboring tissue.

sively infiltrated with cells. The epithelium is generally in process of proliferation and catarrhal desquamation (Fig. 142 *d*). The tubercles consist of close-set masses of cells (*a*), amid which it is seldom easy to distinguish the ordinary tubercle-elements from the products of epithelial proliferation.

357. In the third form of tuberculosis, referred to for distinction's sake as **adhesive tuberculous inflammation,** the extensive inflammatory changes form the chief character. As in other adhesive or plastic inflammations, abundance of young translucent cellular connective tissue is developed and forms false membranes and adhesions between the dif-

ferent parts. Gray or yellow nodules are scattered through the new-formed tissue, and very often there are also yellowish cheesy foci embedded in it or involving the sero-fibrinous films covering the organs.

Tuberculous pericarditis commonly results in complete adhesion of the layers of the pericardium, though cases also occur in which a certain amount of liquid, cellular, or fibrinous exudation persists in the cavity of the sac. The new-formed tissue of the adhesions consists of delicate grayish-red granulations interspersed with dense fibrous bands, and contains gray or yellowish discrete tubercles as well as larger continuous caseous masses.

Tuberculous pleurisy is most frequently met with in connection with tuberculous disease of the lungs. Here too the tubercles are seated either in the young vascular connective tissue or in the dense fibrous cicatrices which are formed. A certain amount of sero-fibrinous effusion is usually present; while the larger diffuse caseous masses are rarely seen.

Tuberculous peritonitis is characterized by an abundant development of fibrous tissue, which forms adhesions and false membranes around and between the abdominal viscera. The omentum and mesentery are always more or less thickened; the former is often transformed into a thick hard nodulated mass, or a mere distorted rope crossing the cavity of the abdomen. The new-formed fibrous tissue, and the thickened and infiltrated serous membrane itself, are beset with tubercles and caseous patches in varying numbers. There may or may not be a liquid effusion.

CHAPTER XXXIV.

TUMORS AND PARASITES OF SEROUS MEMBRANES.

8. **Primary neoplasms** are not often met with in the serous mem-s. Some of them belong to the epithelial, and some to the connec-issue class. Of the former the most interesting are the tumors to described as **endothelial cancers** (WAGNER, SCHULZ, BIRCH-HFELD, NEELSEN). They affect the pleura and less often the neum, and generally take the form of multiple flattened nodular hs, white in color, and either isolated or connected by neoplastic , the intervening serous membrane being more or less thickened. tain amount of serous or sero-fibrinous effusion is usually present. rowths give rise to metastasis; and in the case of the pleura these lary growths chiefly affect the peribronchial fibrous tissue, the hial glands, and the muscles of the thorax.

ie tumor is characterized by the presence in it of nests and clusters thelial cells (WAGNER, SCHULZ, NEELSEN) which at the periphery growth have often a columnar appearance. The nests and clus-ie in a dense fibrous stoma, and follow exactly the course of the iatic vessels. They are usually said to arise from the multiplica-f the endothelial cells of the lymphatics, but this appears to be very ful. As it can be shown that the surface epithelium of the serous rane is in a state of active proliferation (NEELSEN), and gives rise it to some of the columnar elements of the growth, it is more nat-o refer the development of the neoplasm generally to the prolifera-f the epithelium of the primitive body-cavity (Art. 348), and thus kon it as a genuine carcinoma.

broma and myxoma are the commonest of the connective-tissue tu-but even they are rare; sarcoma is very rare. WALDEYER has bed a single case of plexiform angiosarcoma of the peritoneum.

imors of the subserous tissue are more common, especially fibroma, i, and sarcoma. Tumors of the mediastinal tissue are compara-common, and may reach a very great size.

condary growths are much more frequent than primary ones. rs of the peritoneum follow from primary growths in the abdominal i; cancers of the pleura from growths in the mamma or thyroid Cancer of the œsophagus and stomach may affect the pericar-by direct extension, or by giving rise to metastatic nodules.

Metastases generally take the form of definite nodes or nodules. In the pleura they lie chiefly along the course of the pleural and subpleural lymphatics. According to the texture of the parent growth, they are soft and white or medullary, hard and scirrhous, or occasionally brown or black, that is to say melanotic. The surrounding tissue may be but slightly affected, or it may be thickened, hyperplastic, indurated, and full of new vessels. When the nodes lie thick together the affected region (such as the omentum) may be changed into a thick dense tuberous mass.

Less frequently the growth is indefinite or diffuse. This is the case however with colloid cancer of the intestine or ovary, which may attack the peritoneum by direct extension and fill the entire abdominal cavity with gelatinous masses.

Dermoid and teratoid tumors (fœtal inclusions) are comparatively rare in the peritoneal region. The former are chiefly met with in women, and are seated in the ovary or its neighborhood. Fœtal inclusions (Art. 13) may occur in various sites, and take the form of cysts adhering to the surrounding organs and containing fœtal rudiments.

Serous **cysts** are generally found in connection with the female generative organs. Occasionally cysts of various sizes occur in other parts of the abdomen, but their mode of origin is not yet sufficiently known. They contain a highly albuminous liquid, which is sometimes viscid and mucous in consistence.

Of the **animal parasites** the echinococcus is of some importance. It may form hydatid cysts of considerable size in the serous cavities, and the cysts are often adherent to the surrounding parts. Cysticerci are occasionally met with, but they seldom give rise to any notable disturbance. Sometimes intestinal parasites, such as round-worms, escape into the peritoneal cavity either through some pre-existing wound of the intestine or by direct penetration. The consequence is usually a purulent or putrid peritonitis.

Embryos of *Trichina* pass from the intestine into the peritoneal cavity; they do not however remain there, but pass on into the muscles.

References on cancer of the serous cavities:—WAGNER, *Arch. d. Heilk.* XI.; E. SCHULZ, *ibid.* XVII. BIRCH-HIRSCHFELD, *Path. Anat.*; CHURCH, *Trans. Path. Soc.* 1870; BOSTROEM, *Deutsch. Arch. f. klin. Med.* XXIX.; BÖHME, *Virch. Arch.* vol. 81; NEELSEN, *Deutsch. Arch. f. klin. Med.* XXXI.; G. DE MASSY, *Gaz. d. Hôpitaux* 1867; GROSS, *Philadelphia Med. Times* 1878; HUBL, *Wien. med. Woch.* 52, 1879; THIERFELDER, *Atlas d. path. Histologie* Plate XXII.

SECTION V.

THE SKIN.

CHAPTER XXXV.

INTRODUCTORY.

359. **The skin** is a somewhat complex structure, which fulfils not merely the passive office of covering and protecting the organism, but also certain active functions of an important kind. It serves as an organ of touch, as a regulator of the body-temperature, as a secretory organ with a definite secretion, and as an excreting and absorbing organ subserving among other purposes the adjustment of the gaseous constituents of the tissues. In accordance with the nature of its physiological functions it is in close relation both with the tissues and with the outer world. No other organ in the body has so many different tasks to perform, and none is so constantly exposed to extraneous influences.

Its close relations with the rest of the body and with the outer world account sufficiently for the fact that it is especially liable to disease and injury. The mechanical, thermal, and chemical influences to which it is perpetually exposed often induce in it morbid changes, chiefly of the inflammatory kind; while vegetable and animal parasites settle in it and affect it injuriously in various ways. The disorders which are induced by the direct action of injurious agents are classed as **idiopathic skin-diseases.**

In like manner the skin may be affected by morbid influences from within, arising from changes in the blood or the juices, or indirectly from disorders of the heart, liver, kidneys, genital organs, nervous system, etc. Disorders which appear as the manifestation or the result of a primary disorder having its chief seat elsewhere are classed as **symptomatic skin-diseases.**

In view of the endless variety of injurious agencies by which the skin may be affected, it is plain that no good end can be served by treating the pathology of the skin on purely ætiological lines. Moreover, the fact that the same injury may give rise in different individuals to very different affections, and that conversely different injuries may produce the same ultimate effect, affords another reason against the classification of skin-diseases according to their causes alone.

In the following chapters we shall classify the diseases of the skin in the main according to the histological changes which they involve. Ætiology will be appealed to as a subsidiary principle of classification in affections where (as in parasitic disease) the exciting cause either is itself

amenable to microscopical investigation, or always induces the same specific textural change. The histological mode of classification cannot of course be always carried out with perfect strictness. The above-mentioned fact—that the same morbid change may be produced in various ways and may thus appear as a stage in various distinct morbid processes—obliges us now and then to have regard to the general clinical course of a disease as well as to its histology. And as in the case of the skin we can follow without difficulty the evolution and progress of the morbid processes, and so ascertain that the same phase of textural change is not always associated with the same disease (as indicated by its clinical course), we are constrained to modify somewhat the subdivision of the subject which mere pathological anatomy would suggest.

References to the most recent works on the subject:—KAPOSI, *Path. und Therapie d. Hautkrankheiten* Vienna and Leipzig 1880; HEBRA and KAPOSI, *On Diseases of the skin* (New Syd. Soc.) London 1866–1880; NEUMANN, *Text-book of skin diseases* (trans. by PULLAR) London 1871 and *Lehrbuch d. Hautkrankheiten* Vienna 1880; BEHREND, *Lehrb. d. Hautkrankheiten* Berlin 1883; DUHRING, *Diseases of the skin* Philadelphia 1882; *Vierteljahrsschrift f. Derm. u. Syphilis* I.–VIII.

CHAPTER XXXVI.

DISORDERS OF CIRCULATION.

361. The activity of the circulation in the skin varies greatly even under physiological conditions, and its pathological variations are equally remarkable. **Hyperæmia** of the skin may be diffuse or circumscribed, and gives rise to a redness that disappears under the pressure of the finger. The tint varies from pale rosy-red to dark blood-red or the livid purple of cyanosis. The congestion or engorgement of the vessels is limited almost entirely to the upper layers of the corium and especially the papillary layer. The hyperæmia may be active or passive. Active hyperæmia depends upon local injury (and is therefore idiopathic), or upon vaso-motor influences (and therefore symptomatic). Spots of hyperæmia when small constitute **roseola,** when large and diffuse **erythema.** Sometimes the hyperæmic parts are also notably swollen and the tissues saturated with transuded liquid; this is the case in inflammatory œdema (Art. 24). When the hyperæmia persists for a time the epidermis is loosened and shed, and we have desquamation. And after the hyperæmia has disappeared, especially if it has lasted any time or has frequently recurred, a certain amount of pigmentary discoloration remains, due to the transformation of the extravasated red corpuscles into pigment. After death simple hyperæmia usually leaves no trace on the skin. Engorgement or passive hyperæmia generally gives rise to ill-defined bluish-red blotches. A small spot is called a **livor** or **livedo,** a more diffuse lividity constitutes **cyanosis.**

Anæmia of the skin is manifested by its abnormal paleness, and may be local or general. It may be due either to direct external influences, or to stimulation of the vaso-constrictor nerves.

Œdema of the skin, that is to say saturation of it with serous liquid, is due either to engorgement of the veins or lymphatics, or to increased permeability of the walls of the vessels. Œdematous skin is thick and puffy, and liquid runs from it when it is cut; in extreme cases the epidermis rises in blisters or blebs (Art. 370) from the papillary layer.

Active hyperæmia is not always easy to distinguish from inflammation, into which it often passes as a second stage. The erythematous affections (such as those due to mechanical injury, to heat, etc., and those occurring symptomatically in connection with dentition, dyspepsia, etc.) are usually accompanied by a certain amount of inflammatory exudation.

Acne rosacea is characterized by bright-red spots, nodules, and tuberosities containing dilated blood-vessels, which develop slowly over the surface of the nose and cheeks. Its growth is due to long-continued distention of the cutaneous vessels, sometimes associated with enlargement of the sebaceous glands.

361. Recent **hæmorrhages** in the skin give rise to red stains which do not disappear when pressed with the finger. When they form small irregular specks they are called **petechiæ,** larger elongated or ramified streaks are called **vibices,** and still larger irregularly shaped stains are called **ecchymoses.** When the hæmorrhage gives rise to a nodular or papular irregularity of the skin, it is called **lichen hæmorrhagica** or **purpura papulosa**; when the extravasated blood is collected into a tumor or raised patch it is described as an **ecchymoma** or **hæmatoma;** when it raises the epidermis into a large vesicle or bleb it is a **hæmorrhagic bulla** or blood-blister.

The seat of hæmorrhage varies; usually it is in the corium and papillary layer, and thence the extravasated blood passes up under the epidermis and either raises it from the underlying layers or penetrates among its cells. If the blood gains entrance to the sweat-glands and escapes through their ducts, we have **hæmatidrosis** or bloody sweat.

The changes passed through by the coloring matter of extravasated blood (Art. 68) may be followed with the naked eye in the case of cutaneous hæmorrhages. The bright red of recent blood passes through bluish-red and yellowish-green into brown. After a time the discoloration disappears as the pigment is absorbed, and the altered blood which has penetrated between the epidermal cells comes to the surface and is shed with them.

Cutaneous hæmorrhages are distinguished into idiopathic and symptomatic. Spontaneous hæmorrhages are grouped together under the general name of **purpura.**

The spontaneous or purpuric hæmorrhages are symptoms or consequences of certain affections, some of which are at present ill-understood. The hæmorrhages which accompany some forms of small-pox (variola hæmorrhagica or **purpura variolosa**) may become very serious indeed. They begin as small irregular specks which in a few hours expand and coalesce into great blood-stained patches. Plague, bites of serpents, septicæmia, scarlatina, endocarditis, and other infective and toxæmic conditions are often accompanied by cutaneous hæmorrhages in the form of petechial or livid spots, due to changes in the blood or in the vessel-wall, or occasionally to embolic lodgments of bacteria in the arterioles of the skin.

Purpura (peliosis) **rheumatica** is a peculiar affection which sets in with pains in the knees and ankles, generally accompanied by slight fever; presently large and small ecchymoses appear in the neighborhood of the knees; the exciting cause is unknown. We know as little of the cause of **purpura simplex** and of **purpura hæmorrhagica** (*morbus maculosus Werlhofii*), diseases in which, along with fever and loss of strength, hæmorrhages of the skin appear in various parts of the body. In the latter affection, which is occasionally fatal, the ecchymoses may be as large as the hand or larger, and copious bleeding from the mouth, nose, pharynx, and mucous membranes generally, may ensue.

The hæmorrhages in scurvy or **purpura scorbutica** are usually very grave, and take place not merely into the skin but into the subcutaneous tissues and gums. The affection is nearly always attributable to insufficient or improper food.

The lower limbs of aged patients are sometimes covered with circumscribed petechiæ (**purpura senilis**) depending on atheroma of the arteries and the disturbances of circulation to which it gives rise.

S. MACKENZIE, in a paper *On the nature of purpura* in the *Brit. Med. Journ.* 2, 1883, discusses the present state of our knowledge regarding it, and gives full references to previous works. In a case of purpura hæmorrhagica observed by RUSSELL, WATSON CHEYNE (*ibid.*) found the ruptured capillaries crammed with colonies of bacilli.

CHAPTER XXXVII.

DISCOLORATION AND ATROPHY OF THE SKIN.

362. **Discolorations** of the skin may be diffuse or circumscribed. They are due either to an increase of the natural pigment of the rete and corium (pigmentation proper), or to the deposit of abnormal pigment derived either from without or from some intrinsic source such as extravasated blood (dyschromatosis or staining).

Certain abnormal **pigmentations** are congenital and take the form of brown or black spots of various size. They are called **nævi pigmentosi** or moles: *nævus spilus* is soft and smooth; *nævus verrucosus* is rough and warty; *nævus pilosus* is hairy (Art. 398).

Acquired pigmentations are described generally as **chloasmata** and are either idiopathic or symptomatic. Freckles and sun-spots (**lentigines** and **ephelides**) are examples of the former; they are brownish or yellowish irregular specks from the size of a pin's head to that of a pea. Sun-spots occur chiefly on the face in young people and disappear with advancing years. True or 'cold' freckles have no favorite seat and persist during life (Art. 398).

Pigmentation is often a result of frequently recurring hyperæmia and inflammation, such for instance as are produced by excessive scratching (traumatic chloasma), or long-continued exposure to the sun (sunburn).

Disorders of the viscera, and especially of the uterine system in women (**uterine chloasma**), may be followed by discoloration of the skin; and the skin of marasmic patients is often remarkably pigmented.

Addison's disease is an obscure affection in which the skin assumes a brown or bronze-like hue (*cutis ænea*), and the patient falls into grave cachexia. The bronzing of the skin is said to be connected with the changes in the suprarenal bodies often observed in the disease; but it may be present when the suprarenals are healthy (see BURGER, *Die Nebennieren* Berlin 1883).

In these affections the pigment is met with partly in the deepest layers of the rete mucosum, and partly in the corium. It takes the form of brown or yellow granules, but sometimes the cells are uniformly stained.

The **dyschromatoses** are to be distinguished from true pigmentations; they are due to staining of the corium with various coloring-matters derived from the body itself or from without. Icterus or jaundice

is one example, the skin being stained with bile; argyria or silver-staining due to the long-continued medicinal use of salts of silver, and tattooing, are others. In **jaundice** the skin may be of any shade from lemon-yellow to dusky yellow or green; in **argyria** it may vary from slate-color to brown, the dark granules of reduced silver lying chiefly in the cutis. In **tattooing** the skin is pricked with needles till it bleeds, and coloring-matter, such as charcoal, gunpowder, cinnabar, Prussian blue, or indigo, is then rubbed in; a certain amount of the granular insoluble pigment is retained and remains in the cutis.

363. **Simple atrophy** implies a loss of substance in the several constituents of the skin, generally associated with some change of their structure. It may be localized or general, secondary or primary.

In the physiological retrogression of old age or senile atrophy, certain textural changes take place in the skin which may occasionally become very highly marked. The skin becomes thinner, owing to the alteration of the papillary layer; in some spots where they are normally small the papillæ may disappear entirely. The fibrous bundles of the corium become scanty, and often look turbid or granular in texture, the granules not disappearing in preparations put up in Canada balsam. The structure of the fibrous bundles may be visible or obscured; the latter effect being due to a kind of hyaline degeneration by which the bundles take on a swollen glassy look, not unlike that of solidified jelly (NEUMANN). The vessels of the skin are here and there obliterated, so that in injected preparations the meshes of the capillary network appear abnormally wide. Deposits of pigment in the form of yellowish-brown or dark-brown granules are often observed, and these lie either in the cells of the rete or around the vessels of the cutis.

364. The changes in the cutis are accompanied by corresponding changes in the epidermis. The softer strata become thinned out, so that the horny layer is separated from the papillæ only by a few layers of cells. The horny layer is dry and brittle, and often scaly or branny (**pityriasis tabescentium**). Here and there aggregations of the epidermic scales take place, forming whitish patches of various sizes.

The hairs fall out and are not renewed, the hair-follicles being either empty or producing only a kind of down. Several downy hairs may spring out of one follicle, being developed from a single papilla successively, or from several papillæ seated in secondary saccules within the chief follicle. The follicles may be shrunken and atrophied (Fig. 143 *b*) or distended with accumulations of epidermal cells mixed with small hairs (*c*); in many of them the papilla disappears altogether. The shrunken follicles are cylindrical or conical, or distorted and sacculated. It often seems as if the root-sheath were attempting to bulge here and there into new follicles. When the follicle is much shortened it simply looks like the duct of a sebaceous gland. The follicles are hardly ever entirely destroyed (NEUMANN); even when the root-sheath disappears

the pit or sacculation remains, and is often crammed with cornified epidermal cells.

A certain number of the sebaceous glands disappear from the denuded atrophic patches; others are stunted and shrunken; and others again are distended with retained secretion into cysts (Fig. 143 *d*) which may grow to some size (**milium** or **grutum**); they occur chiefly in places which have been covered with hair, such as the scalp.

The sweat-glands are not perceptibly altered.

Localized atrophies of the skin in the form of whitish streaks and patches are frequently observed in persons of mature age over the buttocks, the trochanters, the anterior margin of the pelvis, the knees, etc. Women who have been pregnant usually have shining white streaks (**lineæ albicantes**) on the surface of the abdomen, and sometimes on the thighs and buttocks. According to LANGER (*Anzeiger d. Gesell. d. Aerzte in Wien* May 1879, *Lond. Med. Record* 1880) in such streaks the fibrous bundles of the cutis are stretched but not ruptured and the

FIG. 143. SENILE ATROPHY OF THE SKIN.

(*Section from a highly degenerate part of the skin of the forehead; the hair-follicles are shrunken and contain epidermal cells and retained sebum; after NEUMANN.*)

a, cutis with turbid granular spots in it.
b, shrunken hair-follicle with the outer root-sheath.
c, cornified cells filling the hair-follicle.
d, distended sebaceous gland

papillæ are more or less obliterated. The white color is due not so much to the thinning of the skin as to the parallel arrangement of the fibrous bundles. The white patches which follow upon anasarca are of a like nature.

Cutaneous atrophies may be produced by pressure, either from within as when tumors force their way through, or from without as when callous parts press or rub upon other parts. Chronic inflammations and certain neuroses also lead to cutaneous atrophy, which has the same general characters as that described in the text.

Xeroderma or parchment-skin is a peculiar affection described by HEBRA and KAPOSI (*Diseases of the skin* III.) which occurs in two main forms. In one the skin is dotted over with smooth spots of yellowish-brown, red, and white; the epidermis is thin dry and parchment-like, being either smooth or furrowed and wrinkled; the cutis is thin and tightly stretched, shrunken, and devoid of fat: the affection is met with chiefly in children, and is progressive. In the other

form, which is stationary, the skin is white and tense; and the epidermis is thin and shiny and comes off in glistening scales.

365. Atrophy of the cutaneous pigment (**achroma** or **leukopathia**) may be a congenital or an acquired affection. When congenital it is described as albinism; when acquired as vitiligo or *leukoderma acquisitum*. General or universal **albinism** consists in congenital absence of all the normal pigment of the body. Albinoes have a milk-white or pinkish skin; their hair is yellowish-white and silky, the iris and choroid are uncolored, and therefore show the red tint of the blood they contain. Albinism is not very common among Europeans, but it is common enough among negroes. Partial albinism also is often seen in negroes; they have one or more patches of white on the body, but the eyes are not devoid of pigment.

Vitiligo sometimes appears without any discoverable cause. Some cases seem to be connected with certain changes in the cutaneous nerves (LELOIR, *Arch. de physiol.* 1881). It takes the form of white or pinkish patches surrounded by a zone of increased pigmentation. Occasionally by the growth and coalescence of new patches the affection may extend over a considerable extent of the skin.

White spots may follow upon inflammatory affections of the skin, such as boils, lupus, syphilitic eruptions, leprous growths, etc.

Atrophy of the pigment of the hair (**canities** or poliosis) is a physiological phenomenon when it occurs in advanced age. The pigment-granules in the cortical substance of the hair diminish in number; but this is because the formation of pigment in the bulb is arrested (KAPOSI), not because the pigment already existing in the hair is destroyed.

In premature grayness the process is the same.

CHAPTER XXXVIII.

INFLAMMATIONS OF THE SKIN.

c. Transitory eruptions with slight exudation: erythema, papulæ, urticæ.

366. In speaking of **erythema** as a form of simple cutaneous hyperæmia (Art. 360) we pointed out that any intensification of the process might lead to exudation, and so transfer the affection from the category of hyperæmia to that of inflammation or **dermatitis.** There is no very obvious difference in appearance between erythematous hyperæmia and erythematous inflammation, except it be that in the latter the affected part is somewhat swollen. If the exudation is confined to the region of a few papillæ, or is at least more intense at some spots than at others around them, the swelling takes the form of small circumscribed solid elevations known as **papules** or *papulæ.* If the group of swollen papillæ is larger, the flattened elevations then formed are called **wheals** or *urticæ.* When the exudation is still more abundant the irregular prominences are called **tubercules** or *tubercula.* Wheals and tubercules often become pale at the centre while the margin is still hyperæmic.

Microscopic examination shows that these swellings are mainly due to serous exudation, which distends the meshes of the corium and papillary layer and causes the cells of the rete mucosum to swell up. More intense and more enduring inflammation is accompanied by greater extravasation of cells, so that the fibrous tissues appear infiltrated with leucocytes.

The swelling of the individual cells of the rete sometimes results in the liquefaction and destruction of some of them, in which case the papules and wheals are transformed into **vesicles** (Art. 370). The exuded liquid often contains red corpuscles; in this case the redness of the spot does not wholly disappear when pressed with the finger, but a certain amount of reddish or brownish staining remains.

The effect of such inflammations on the skin is generally very slight. The exudation being mainly liquid is readily and speedily re-absorbed, and there is often nothing left to indicate the existence of the affection. In some cases the surface layers desquamate in the form of thin scales and shreds, or if hæmorrhage has occurred some slight pigmentation remains, though this also disappears after a short time.

367. The **causes** of these slight inflammations are exceedingly various. They occur after external injuries of many kinds, as accessory symptoms in certain infective diseases, and in affections of the internal organs. Frequently no cause at all can be assigned; now and then they seem to be due to a neurosis of the vaso-motor mechanism.

Special mention must be made of the following forms, among the many which occur; they are distinguished by their special course and symptoms.

(1) The eruption of **measles** (*morbilli, rubeola*) appears first on the face, forehead, and temples, and thence extends over the back of the neck, the shoulders, and the trunk. It forms dull red or raspberry-colored patches of the size of the finger-nail or larger, with a tendency to crescentic grouping; the patches are either level with the skin, or slightly raised into papules corresponding to the openings of the hair-follicles. The skin and subcutaneous tissue, especially in the face, are somewhat swollen and œdematous. The patches may run together here and there but they never become quite confluent. In a few hours after its appearance the eruption becomes pale, leaving the skin faintly yellow; and presently a slight branny desquamation follows.

(2) The eruption of **scarlatina** appears first on the neck and clavicular region, and thence extends over the back and breast to the limbs. At first it takes the form of minute red dots closely crowded together and giving the skin a diffuse or uniform tint. The tint is at first pink, afterwards deep red, livid, or scarlet. The skin is swollen and infiltrated. The eruption lasts one to three days, and occasionally as long as six or seven; it then fades and leaves the skin stained of a yellowish-brown. Afterwards the epidermis desquamates in flakes and scales of various sizes; if the flakes are large the desquamation is called membranaceous, if small and thin it is furfuraceous. Occasionally the eruption is papular, tubercular or vesicular (*scarlatina papulosa, vesicularis, pemphigoides*), and not infrequently it is hæmorrhagic (*scarlatina hæmorrhagica*). The exudation poured out into the connective tissue is somewhat rich in cells.

(3) **Erythema exudativum multiforme.** According to KAPOSI this affection begins as an eruption of flat slightly-prominent circumscribed and scattered spots (*erythema læve*) on the back of the hands and feet and the neighboring parts of the arm and leg. The spots are at first the size of a pin-head but presently grow to that of a pea; they are vermilion in color and turn pale when pressed. They grow at the margins while the centre becomes depressed and cyanotic; the larger spots may become confluent. Hæmorrhages not infrequently occur. As the red margin extends and the centre fades we have *erythema annulare*; if several rings encroach on each other we have *erythema gyratum*; a red spot surrounded by a pale zone and that by a red zone constitutes *erythema iris*; if the eruption becomes papular it is *erythema papulatum*; if there are wheals it is *erythema urticatum* or *lichen urticatus*; if vesicles are formed *erythema vesiculosum*. If the formation of vesicles goes on at the margin while the centre recovers we have *herpes circinatus*, characterized therefore by its ring of vesicles; if a vesicle persists in the centre it is *herpes iris*. Erythema with large blebs or bullæ is *erythema bullosum*. A brown pigmentation usually remains behind after the eruption declines. When vesicles have formed scales and scabs are left. The affection lasts from two to four weeks; its cause is unknown.

(4) **Erythema nodosum** (*dermatitis contusiformis, urticaria tuberosa*) is characterized by the formation of large blotches or rounded nodes usually on the lower limbs. It is sometimes ushered in by slight fever. The blotches are slightly elevated or not at all, and are bright red at the margins and purple at

the centre. In two or three days they begin to fade, passing through tints of blue, yellow, and green. The exudation being chiefly serous absorption is rapid, and the affection leaves nothing behind it but a slight staining of the skin.

(5) **Traumatic erythema** is produced by irritation of the skin, mechanical, thermal, or chemical. Mechanical irritation is exemplified by the friction of clothes or of two parts of the body in contact; the effects of thermal irritation by burns or frost-bites of the first degree; chemical irritants are such as turpentine, mercurial ointment, dilute acids, and the poison of insect-stings. The cutaneous inflammations or swellings induced by frost are called **chilblains** or *perniones*. Erythema is an occasional result of the use of certain medicaments such as quinine, copaiba, or belladonna (VAN HARLINGEN, *Arch. of Dermatology*, 1880; DUHRING, *Diseases of the skin* Philadelphia, 1882; LEWIN, *Untoward effects of drugs* Detroit, 1883).

(6) **Roseola**, or the rash of circumscribed red spots which occurs in connection with certain general disorders of the system, is allied to the exudative erythema. It is described, from the condition with which it is associated, as *roseola rheumatica, choleraica, typhosa, æstiva, infantilis, etc.*

(7) **Pellagra** (*mal rosso, mal del sole, risipola lombarda*, Lombardian leprosy) is a peculiar disorder met with in the north of Italy, Southern France, Spain, and Roumania. It appears as an erythematous rash on the exposed parts of the body in spring and summer, and disappears in autumn with desquamation of the epidermis. Marked disturbance of the health may occur; the patient becomes debilitated, and nervous symptoms often follow. The disease is apt to recur in succeeding years (MAYR, *Hebra's Diseases of the skin* (New Syd. Soc.) I.; KAPOSI, *Path. u. Therap. d. Hautkr.* Vienna and Leipzig 1880; SCHEIBER, *Viertelj. f. Derm. u. Syph.* II.; WINTERNITZ, *ibid.* III).

(8) **Urticaria** or nettle-rash is an eruption of wheals which rise and disappear very suddenly. The wheal is white or yellowish, and is bordered by a zone of red. Sometimes small vesicles or papules are formed. The rash is either caused by external irritation (such as the stings of nettles, of jelly-fish, or of insects), or it is a symptom of some irritation elsewhere, especially in the alimentary canal.

b. Eruptions with considerable exudation: tubercula, squamæ, vesiculæ, pustulæ, crustæ.

368. The affections we have next to consider are described collectively as **phlyctænoses**, and are distinguished from the erythematous eruptions by the more intense character of the inflammatory changes involved. In many of them moreover the duration of the affection is greater, and recovery is less easy or less complete.

The inflammatory infiltration may be diffuse or circumscribed. In recent eruptions the cellular exudation lies chiefly in the neighborhood of the veins. Degenerative changes in the epidermal cells and fibrous tissue may precede, accompany, or succeed the exudation. In later stages proliferation of the cells and fibrous tissue is set up, and brings about repair or hyperplasia as the case may be. The **efflorescence** or mode of appearance of these inflammations of the skin is very various.

The infiltration may be local and circumscribed, forming papules; or it may be extensive and diffuse, giving rise to remarkable swellings. The epidermal layers may be beset with vesicles, pustules, scales, crusts, or

scabs; or there may be loss of part of their substance, and the exudation may be poured out on the free surface.

The varieties of cutaneous inflammation or dermatitis such as we are considering differ widely in their general clinical course. Some are acute, others are chronic and occasionally last for years. Their exciting causes are likewise exceedingly various, so that it is difficult to lay down any general proposition with regard to their ætiology.

369. The **exudation**, whether localized or diffuse, consists of liquid, of coagulated fibrin, and of cells. The latter are the most easily recognizable constituent, and in hardened sections are often the only one which the microscope can detect. In slight cases the exudation may be limited

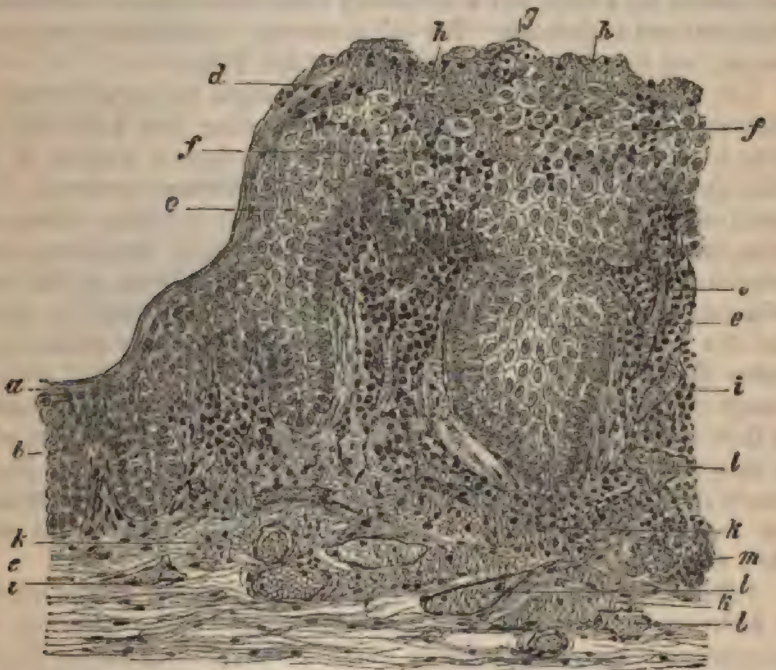


FIG. 144. SECTION THROUGH A SYPHILITIC MUCOUS PATCH.
(*Aniline-brown staining:* × 100.)

a, horny layer of the epidermis.
b, rete Malphigii.
c, corium.
d, horny layer swollen up and infiltrated with leucocytes.
e, swollen cells of the rete Malphigii.
f, swollen epidermal cells infiltrated with cells.
g, degenerate epidermal cells into which leucocytes have penetrated.
h, granular coagula.
i, swollen and infiltrated papilla.
k, corium infiltrated with cells and fibrin.
l, lymphatic vessel.
m, sweat-gland.

to the neighborhood of the papillæ (Fig. 144 *i*); in other cases the cutis (Fig. 144 *k* and Fig. 146 *m*) and even the subcutaneous tissues are thickly infiltrated; and the epidermis may also (Fig. 144 *f g h*) be saturated with exuded liquid.

The proportion of extravasated cells in the exudation may be small or large. Recent and copious exudations (Fig. 145) are usually poor in cells, older and slowly accumulating exudations are richer (Figs. 144 and 146). When the exudation coagulates (Fig. 144 *k*) granular and fibrous masses are formed. The liquid effused into the connective tissue lies partly in the lymph-spaces and meshes, partly in the lymphatic vessels (Fig. 144 *l*).

The liquid poured out from the papillæ passes also into the epidermal layers; and the accompanying cells insinuate themselves between the epidermal cells (Fig. 144 *f*), and afterwards actually penetrate them. The epidermal cells become in this way distended (*f g*) or vacuolated (Fig. 146 *e f*), and the protoplasm and nucleus are displaced. The nucleus may persist for a time, but it ultimately either swells up or crumbles into fragments and so perishes. The cell-membrane withstands destruction longest, but it too may at length dissolve (Art. 371).

370. In many cutaneous affections the changes in the epidermal or epithelial cells do not cease with the simple swelling just described, but go on to the destruction and disintegration of a certain number of the cells, and in this way **vesicles** and **blebs or blisters** are produced. The terms vesicle and blister, used in connection with cutaneous inflammations, imply an excavation under the epidermis due to destruction and solution of some of the cells. Blisters are never produced by the mere collection of fluid between the epidermal layers, say between the horny and the mucous layers. But blisters may be formed by transudation under the epidermis by which the whole membrane is raised without change over a definite area. Such blisters or blebs are not inflammatory in their origin; they are due to vascular engorgement, and are met with in cases of extreme œdema of the integument. The transuded liquid simply raises the epidermal from the fibrous stratum. Similar blisters are formed in putrefactive and gangrenous affections of the skin (Art. 42).

Inflammatory vesiculation is always then the result of excavation due to destruction of epidermal cells in the softer layers of the epidermis, the excavations being always more or less fully occupied by exuded liquid. The epidermal cells may perish in various ways. The time and mode in which the cells die, and the consistence and amount of the exudation determine the character of the vesicular eruption. Thus if the cells are directly injured and killed outright (as by high temperature), while the papillary vessels are simultaneously damaged and pour out abundant exudation, the dead cells are very rapidly dissolved and disappear. On the other hand, if the injury primarily affects the vessels of the cutis and papillæ and so induces exudative inflammation, the cells perish slowly and pass through a comparatively prolonged stage of mere swelling.

When a small portion of the skin is exposed for a short time to a high temperature, the first effect is a marked reddening of the surface.

Then the horny layer is raised by the formation beneath it of a cavity distended with fluid, and a blister is produced.

By the heat the epidermal cells are partially destroyed, and the vessels of the cutis are more or less disorganized. The vessels pour out an exudation, which passes from the tips of the papillæ into the epidermal layers. The cells already killed or injured by the heat are thereby swollen up (Fig. 145 *d*), and soon dissolve completely (*f*). This takes place at first immediately over the papillæ (*d f*). The inter-papillary cells (*e*) may hold out for a time; but they are apt to be stretched and distorted by the exudation, and as soon as this becomes sufficiently abundant they too swell up and then dissolve (*g*). Coagulation sets in as the cells dissolve and the place is taken by granular and fibrous masses whose forms correspond in general to the cell-areas, and so maintain for a time the configuration of the rete Malpighii (Fig. 149).

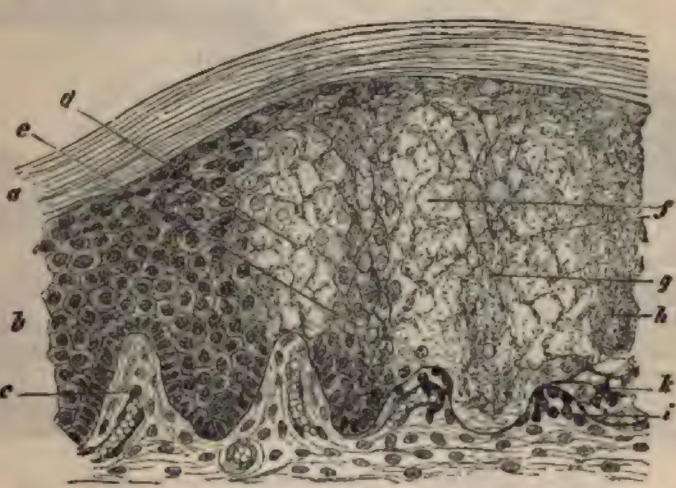


FIG. 145. SECTION THROUGH THE MARGIN OF A BLISTER DUE TO A BURN.

(*Carmine staining:* × 150.)

a, horny layer.
b, rete Malpighii.
c, normal papilla.
d, swollen epidermal cells, in some of which the nucleus is still visible, in others not.
e, inter-papillary cells, those below being uninjured, those above are swollen and stretched and have lost their nuclei.
f, fibrinous mesh-work (composed of cells and exudation; cell-structure altogether lost over the papillæ).
g, swollen denucleated cells.
h, inter-papillary cells separated from the cutis and dissolving.
i, depressed papilla, infiltrated with cells.
k, subepidermal coagulated exudation.

The free and abundant exudation which by its pressure raises the horny layer of the epidermis depresses and flattens the papillæ (*i*). If the exudation continues after the solution and coagulation of the epidermal layers, the entire fibrinous mass may itself be lifted by a new accumulation (*k*) taking place beneath it.

371. The above mode of vesiculation occurs only in cases where the

exudation is sudden and abundant. When the inflammation is less acute and the injury to the epidermis less extensive than it is in burns, the vesicles or blebs are formed more gradually. Thus the erysipelatous inflammation of the skin, which follows upon the lodgment in its lymphatics of certain micrococci (Fig. 146 *h i k*), is characterized by primary cellular infiltration (*m*) of the corium and papillæ. When the exudation reaches the epidermal layers the cells (*f*) begin to swell up; they then become vacuolated, that is to say drops of liquid (*e*) distend them and displace their protoplasm and nucleus. If several vacuoles are formed simultaneously within the same cell, the protoplasm is reduced to a kind of mesh-work (*g*), in which however the nucleus can generally be detected. At length the protoplasm dissolves completely and the nucleus is

FIG. 146. SECTION OF THE SKIN IN ERYSIPELAS BULLOSUM.

(*Alum-carmine staining, mounted in Canada balsam:* × 60.)

a, epidermis.
b, corium.
c, bleb or bulla.
d, roof of the bleb.
e, vacuolated epidermal cell.
f, swollen cell and nucleus.
g g_1, cavities produced by solution of epidermal cells, containing fragments of cells and pus-corpuscles.
h i, lymphatics filled with micrococci.
k, micrococci in the substance of the tissue.
l l_1, necrosed tissue.
m, cellular infiltration.
m_1, fibrino-cellular infiltration.
n, fibrino-cellular exudation within the bleb.

broken up and disappears. The cell is thus replaced by a cavity (*g*) containing liquid. Several such cavities next coalesce by the solution of the cell-membranes, and so larger and larger cavities (vesicles or blebs) are produced. As the several vesicles become more and more distended the cells lying between them, whether healthy or degenerate, become compressed and stretched or otherwise distorted (Fig. 147).

The vesicles of small-pox, herpes, eczema, and many other eruptions are formed according to the same general plan, but with manifold differences in details. The epidermal changes especially are apt to vary; thus in some cases the cells are speedily transformed into homogeneous glassy flakes or into granular coagula, in others the nuclei break up into fragments at an early stage, and so on.

The above account of the process of vesiculation differs in many points from those given in most text-books and in many dermatological memoirs. It lays much more stress than is usual on the disintegration and solution of the epidermal cells as factors in the process

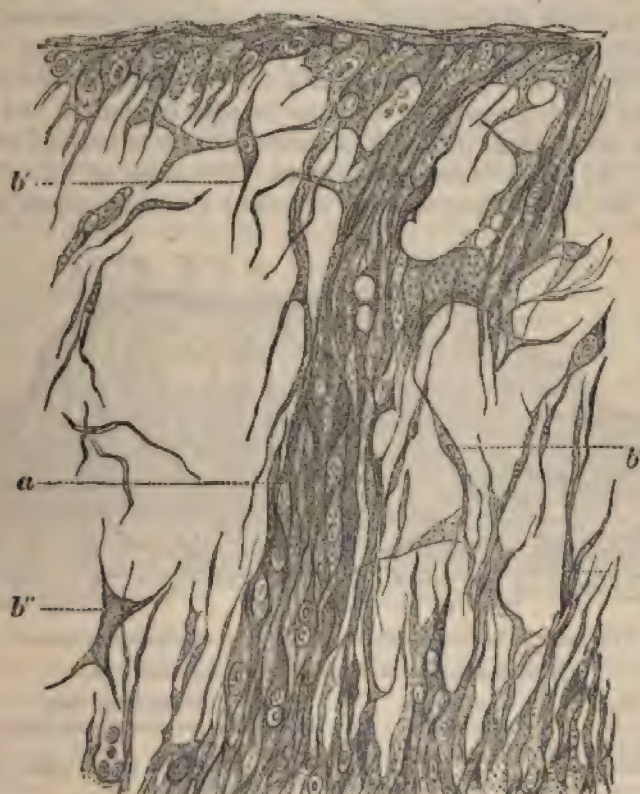


FIG. 147. SECTION THROUGH A VESICLE OF HERPES ZOSTER.

(*From HAIGHT, Sitzungsber. d. k. Akad. in Wien* 1868: × 450.)

a, band traversing the cavity of the vesicle composed of stretched and spindle-shaped epidermal cells.

b, loose mesh-work, composed of spindle shaped cells (b') and stellate cells (b'').

The author claims, however, that the account is the outcome of his own researches and those of TOUTON, who worked under the author's direction. Figs. 145 and 149 are taken from TOUTON'S preparations, and are discussed in his paper entitled *Vergleichende Untersuchungen über die Entstehung der Hautblasen* Tübingen 1882. The student may also refer to the papers of WEIGERT (*Anatomi-*

sche Beiträge zur Lehre von den Pocken Breslau 1874) and UNNA (*Virch. Arch.* vol. 69, and *Vierteljahrsschrift f. Derm. u. Syph.* v.).

372. The vesicles just described are always loculated, owing to their mode of origin. As they arise from a number of contiguous foci of degeneration and solution, fragments of cell-walls and compressed or distorted cells are left stretching across the cavity, and so form partial septa. As the vesicle develops, these septa give way or dissolve one after the other, and the loculi run together (Fig. 148) into a single cavity traversed by mere shreds and fibres.

Meanwhile the contents of the vesicle usually undergo certain changes. The first portions of the exudation into the epidermal layers are generally poor in cells. The cavities contain only a few fragments (Fig. 146 $g\ g_1$) of disintegrated epidermal cells and a few migrated blood-corpuscles. But as the vesicle grows older the latter increase in number, and when it reaches a certain stage its liquid contents become turbid and at length purulent; the vesicle becomes a **pustule**. The stage at which this occurs is a late one in many vesicular eruptions (variola, burns); in others

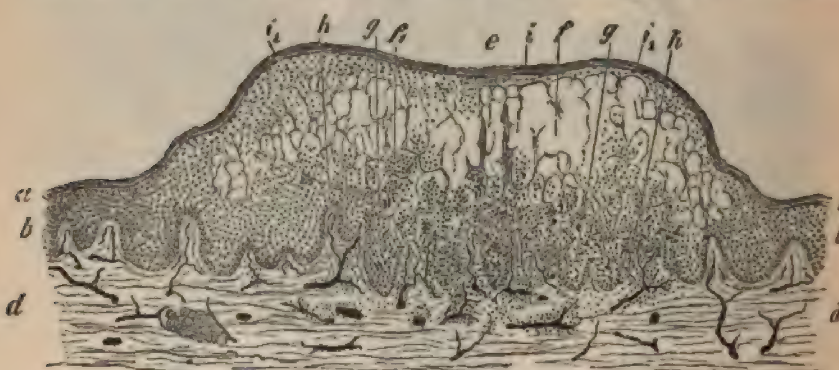


FIG. 148. A SMALL-POX VESICLE PASSING INTO THE PUSTULAR STAGE.

(*Injected preparation stained with hæmatoxylin:* × 25.)

a, horny layer.
b, mucous layer.
d, cutis.
e, the vesicle.
f, cavity of the vesicle.
f_1, pus corpuscles.
g, epidermal detritus and pus-corpuscles lying between the papillæ.
h, papilla infiltrated with cells.
i, umbilication over the thin part of the cap of the vesicle.
i_1, margin of the vesicle where the cap is thicker.

as in eczema, it is early. Sometimes, however, the exudation is purulent from the beginning, and sometimes it contains red corpuscles, so that the contents of the vesicle are blood-stained.

373. When a dermatitis results in infiltration of the epidermis with vesiculation and pustulation, certain other changes usually ensue which lead to the formation of scales, and crusts or scabs.

Scales (*squamæ*) are small bran-like flakes, or larger thin white or

dirty gray glistening lamellæ or plates, or continuous membranaceous shreds, which are shed from the surface of the epidermis. The desquamation is called **furfuraceous** when the scales are branny; it is **membranaceous** when they are larger; and **siliquose** when the scales are chiefly composed of the horny shells of dried-up blebs. The scales occasionally cohere into irregular masses or thick cakes.

The formation of scales depends in part on excessive production and in part on morbid alteration of the corneous cells. The pathological element of the process is this: that the cells forced up from the lower layers of the epidermis to the surface do not pass through the regular stages of cornification, but in consequence of the nutritional disturbance simply become as it were dried up. Scales may likewise be formed in consequence of some morbid change in the secretion of the sebaceous glands (Art. 403).

Crusts or **scabs** (*crustæ*) are formed by the drying of epidermic exudations. They usually result from vesicles and pustules whose contents have ceased to be liquid, but sometimes the primary exudation bursts through the swollen epidermal layers and is effused on the surface of the skin, where it dries. Scabs are often formed from exudations poured out on the denuded surface left after some loss of substance or excoriation of the epidermis, such as is caused by a scratch or graze; and fissures or *rhagades* in the skin usually become covered over with crusts.

If the exuded liquid is serous the crusts or scabs are gum-like; if it contains blood they are brown or black; purulent exudations dry into dirty brownish-yellow scabs. The form and size of the scabs vary with their mode of origin. The skin around them is always somewhat reddened, and their base is swollen.

374. The **issue** of the processes we are considering is generally in recovery and repair, but permanent alteration of the skin is not an uncommon result.

When recovery is about to begin the signs of inflammation gradually disappear, and the exudation ceases. Part of the exuded liquid, namely that within the fibrous tissues, is absorbed; that which lies on the surface, together with the dead and disintegrated epidermal cells, is thrown off, and the defect is made good by regenerative multiplication of the cells around.

The multiplication takes place chiefly along the line where the rete Malphigii borders on the cavity of the vesicle (Fig. 149 *d*); but some share in the process is also taken by the uninjured interpapillary cells, and by the epithelium of the sweat-glands (*h*) and hair-follicles. The process of repair begins soon after the vesicle is formed, in burns it begins on the second day; masses of cells are produced which advance gradually over the denuded and depressed papillæ (*d*). When the multiplication has reached a certain point, differentiation into layers begins to be perceptible (d_1); and often at the margin of the vesicle the layers are complete

even to the horny surface layer, before the central parts are covered over (d_2).

The result of this multiplication and growth is that the vesicle with its contents continues to be thrust upwards, and when the new horny layer is complete it lies as it were between two horny shells, and is generally by this time dried up into a mere crust.

The process is different when part of the cutaneous fibrous tissue, and especially the papillary layer, has become necrosed under the stress of the initial inflammation (Fig. 146 l_1). The gap thus produced is never completely repaired, and a depressed cicatrix remains; the 'pits' that follow the eruptions of unmodified small-pox afford the best example.

Permanent alterations in the texture of the skin are very common after long-enduring or often-repeated inflammations. They are of the nature of hyperplasia, or of atrophy, of the epidermal and fibrous structures.

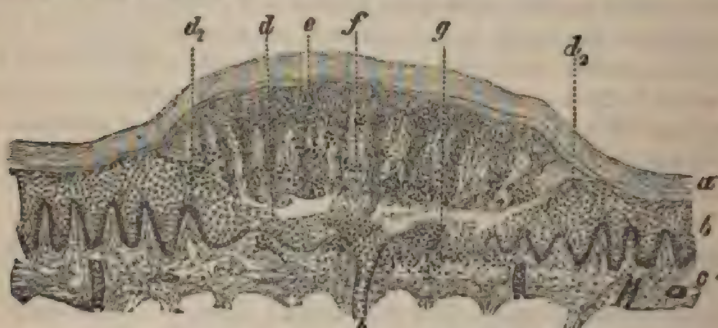


Fig. 149. Blister from a burn in process of healing.

(*Section through the skin of a cat's paw forty-eight hours after a burn: alum-carmine staining, mounted in Canada balsam:* × 25.)

a, horny layer.
b, rete Malpighii.
c, corium.
d, new-formed epidermal cells, undergoing differentiation into layers at d_1.
d_2, new-formed horny layer
e, the old degenerate epidermis
f, pus-corpuscles.
g, secondary exudation.
h, sweat-gland.

In the latter case the epidermis and corium may be notably thinned, and the papillæ depressed and stunted. Hyperplastic changes leave the epidermis, and especially its horny layer, thickened and condensed, while the papillæ and corium grow larger and stouter. *Pityriasis rubra* (Art. 377) is a good example of a cutaneous inflammation ending in atrophy; the thickening that follows chronic eczema (Arts. 385, 413) illustrates the hyperplastic condition.

More or less permanent pigmentation is another common result of moderately intense inflammation of the skin.

375. **Erysipelas** is an acute inflammation of the integument depending upon traumatic infection; it takes the form of gradually extending redness and swelling accompanied by a certain degree of fever. In the

early stages the skin appears tense and shining and of a bright red tint. Presently it becomes more or less livid or brown, the swelling goes down, and the epidermis is thrown off in scales or flakes.

Sometimes the exudation is more copious and tends towards the surface, in which case vesicles and blebs are formed, and the eruption is described as *erysipelas vesiculosum* or *bullosum* (Fig. 150). When the contents of the vesicles become purulent we have *erysipelas pustulosum*, which, as the pustules dry up into a scab, passes into *erysipelas crustosum;* or, if portions of skin become necrotic or gangrenous, into *erysipelas gangrenosum*.

When examined microscopically the erysipelatous exudation is seen to be abundant, serous or fibrinous (Fig. 150 m m_1) and highly cellular, and it infiltrates the entire thickness of the skin and the subcutaneous

FIG. 150. SECTION OF THE SKIN IN ERYSIPLAS BULLOSUM.

(*Alum-carmine staining, mounted in Canada balsam:* × 60.)

a, epidermis.
b, corium.
c, bleb or bulla.
d, roof of the bleb.
e, vacuolated epidermal cell.
f, swollen cell and nucleus.
g g_1, cavities produced by solution of epidermal cells, containing fragments of cells and pus-corpuscles.
h i, lymphatics filled with micrococci.
k, micrococci in the substance of the tissue.
l l_1, necrosed tissue.
m, cellular infiltration.
m_1, fibrino-cellular infiltration.
n, fibrino-cellular exudation within the bleb

connective tissue. The vesicles and blebs are formed (Art. 371) by the liquefaction and disintegration of the cells of the rete Malpighii (*e f g*). The liquefaction commences in isolated spots, and thus the first cavities formed are separated by cells which are more or less stretched and distorted; but as the cavities coalesce these septa break down and disappear (*c*).

The originating **cause of erysipelas** is to be sought in an invasion of micrococci (*h i k*), which gain entrance at some wounded part of the skin (Art. 204). They proceed to multiply within the lymphatics (*h*) and at length completely fill them (*i*). From the lymphatics they pass into the connective tissue, where they form coherent masses (*k*) or chaplets. The tissue around these colonies becomes necrotic (l_1), and presently inflammatory reaction is set up. The extravasated cells may be scattered irregularly through the tissues, or be arranged in elongated clusters.

The extent of the necrosis is often slight, but at times it reaches a considerable magnitude and leads to serious loss of substance, as in gangrenous erysipelas.

FEHLEISEN published quite recently the results of his experiments on the cultivation and inoculation of the micrococci which constitute the virus of erysipelas (*Sitzungsberichte d. Würzburg. phys.-med. Gesell.* 1882). ZIEGLER (*Naturforscherversammlung in Salzburg* 1881) made inoculative experiments (Art. 204) on rabbits, but they all led to a fatal result. FEHLEISEN while confirming ZIEGLER'S work was able to preserve the animals alive, and to watch the process of repair to its issue in complete recovery. He cultivated the micrococci 'purely' on gelatine impregnated with peptonized meat-infusion, and effected a successful inoculation on the human subject with micrococci of the fourth artificially-cultivated generation; perfectly typical erysipelas was induced. After these experiments the specific significance of the micrococci can hardly be doubted.

376. **Psoriasis** is a chronic disease of the skin characterized by the formation of dry glistening white scales. They are piled upon each other in small heaps, or over large discoid patches, which have a definite red slightly raised base that is easily made to bleed (KAPOSI). The eruption begins in minute brownish-red nodules which in a day or two become covered over with epidermal scales. If the scales are removed a bleeding point appears on the reddened base. When the nodules are numerous and discrete the disease is distinguished as *psoriasis punctata;* where the patches and scales are larger we have *psoriasis guttata* and *psoriasis nummularis*.

As the disease passes away the base becomes pale and the scales are shed; the skin may at once assume its normal appearance or remain pigmented for a time. Often the patches heal in the centre while the margins are still advancing; in this case the affection is named *psoriasis annularis* or *gyrata*. The disease may occur at any spot, but it chiefly affects the region of the knee and elbow, the scalp, and the sacral region. Both the hair and the nails may be destroyed in the course of it.

The histological changes induced by psoriasis relate essentially to the epidermal cells, the papillæ, and the upper strata of the corium. The two latter are more or less densely infiltrated with leucocytes; and when the disease has lasted for some time hyperplasia of the superficial fibrous tissue and the papillæ is usually set up. The morbid process may occa-

sionally extend to the deeper layers of the corium and the subcutaneous connective tissue.

As regards the epidermis, the mucous layer and especially the interpapillary parts of it appear overgrown. The cornification of the surface layers of the epidermis is interfered with; the cells as they come to the surface appearing simply to shrivel and dry up, while the mutual cohesion of the layers is loosened.

E. LANG (*Viertelj. f. Derm. u. Syph.* 1879, and *Sammlung klin. Vorträge* 208) announced that a fungous growth was always present in the patches of psoriasis; he named it *Epidermidophyton* and regarded it as the exciting cause of the disease. It formed filaments and spores and was found in the deeper layers of the heaps of scales. ZIEGLER has not been able to verify the discovery, having found nothing in the diseased patches but occasional micrococci, and these can hardly be regarded as the specific virus.

On the histology of psoriasis see NEUMANN (*Med. Jahrb.* 1879), R. ROBINSON (*New York Med. Journ.* 1879), JAMIESON (*The histology of psoriasis* Edinburgh 1879), THIN (*Brit. Med. Journ.* 1, 1881).

377. **Pityriasis rubra,** or general exfoliative dermatitis, is a peculiar affection of the entire skin, the only symptoms of which are marked redness and desquamation; neither papules nor vesicles nor pustules are ever formed (KAPOSI). The scales are sometimes small, but they are often of considerable size. After a time the skin becomes smooth, shining, thin, and tense; the hair falls off; and when the disease has lasted for a year or more, general marasmus and death ensue. The only textural change which has yet been made out is a moderate amount of cellular infiltration in the cutis and papillary layer. No special changes occur in the epidermis, apart from those associated with desquamation; though in late stages some small-celled infiltration may be observed in isolated patches. The skin is generally much atrophied, the rete Malpighii being greatly thinned, while the papillæ are dwarfed, and the corium and its fibrous bundles have much the same look as in senile atrophy (Art. 363). The sebaceous glands and hair-follicles are obliterated.

See HEBRA (*Viertelj. f. Derm. u. Syph.* III.), GEBER (*ibid.* III.), FLEISCHMANN (*ibid.* IV.). For cases see DUHRING (*Diseases of the skin* Philadelphia 1882).

378. **Prurigo** is a disease beginning in infancy and generally persisting throughout life. It consists of often-recurring eruptions of miliary nodules or papules, which are pale or pinkish in color, hard and rough to the touch, and accompanied by severe itching. They may be scattered irregularly over the body, but they are often confined to the extensor surfaces of the limbs, the flexor aspects being quite free (KAPOSI). Around the papules there is a certain amount of cellular infiltration derived from the papillary vessels. When the affection has existed for some time the changes in the skin are more marked, and the inevitable scratching sets up eczematous inflammation.

379. **Papular syphilides** are of two chief kinds, distinguished as

the small papular (or miliary) and the large papular (or lenticular) syphilide.

The **small papular syphilide** or syphilitic lichen consists of small nodules of about the size of a pin-head arranged in clusters or rings; as the eruption fades desquamation takes place, and shallow pits remain in the skin.

The **large papular syphilide** consists of sharply-defined hard nodules as large as a hemp-seed or larger, which increases in size by marginal growth. As they fade and desquamate they leave behind pits, which at first are pigmented but afterwards assume a glistening white appearance. Papules are sometimes formed on the palms and soles, and result in membranaceous desquamation: this constitutes what is called palmar or plantar (syphilitic) psoriasis. The separate papules are recognizable in the earlier stages of the affection, but after a time they coalesce, and diffuse infiltration, with callous thickening of the epidermis, is all that appears.

Mucous patches or *condylomata lata* are also classed with the papular syphilides. They are flattened discoid elevations covered with a moist grayish exudation. They develop from originally discrete papules in parts where folds of skin are in contact and keep each other moist, such as the labia, perineum, anus, scrotum, penis, and axilla, and occasionally the mouth.

A section through such a patch shows that the elevation of the skin is due to an infiltration extending (Art. 369) to the epidermis (Fig. 151 *f g h*), as well as into the papillary layer (*i*) and corium (*k*). The exudation consists of leucocytes and fibrin (*h k*), and its presence causes the papillæ to be greatly enlarged and the epidermal layers to be greatly thickened. The latter effect is increased by an increase in the productive activity of the epidermal cells. The patch may disappear by the absorption of the cellular and liquid exudations, and the incrustation and shedding of the diseased epidermis. The swelling first goes down in the middle of the patch, while the margins still remain infiltrated. The affected tissue disintegrates and suppurates, giving rise to an ulcer with infiltrated margins; and as this dries up a crust is formed which is ultimately shed. With reference to the primary syphilitic affection see Art. 391.

The various skin eruptions of syphilis differ remarkably in appearance. A small papular syphilide seems to have little in common with a mucous patch, or a pemphigoid syphilide (Art. 386) with a papular eruption or a hard sore (Art. 391). Yet in all these cases the fundamental processes are closely related, and differ simply in degree and extent. In all of them the essential part of the process is the induction of circumscribed inflammations accompanied by a comparatively abundant cellular exudation. The exudation usually shows no sign of commencing organization, but is either re-absorbed, or cast off with the necrosed and disintegrated tissue in which it lies. Even when the seat of inflammation

attains the form and texture of a patch of granulation-tissue (Art. 391) suppuration and disintegration usually supervene.

The essential element of the syphilitic eruptions is the papule; the consecutive appearance of scales or vesicles or pustules is of secondary importance, as are also the mere size or extent of the affected area.

380. **Lupus erythematosus** is a disease which begins with an eruption of raised red specks or spots (KAPOSI). They are depressed in the centre, or glistening and scar-like, or capped with a thin adherent scale. The reddened margin advances gradually while the centre becomes scarred over, and thus in the course of some months a red-bordered disc

FIG. 151. SECTION THROUGH A SYPHILITIC MUCOUS PATCH.

(*Aniline-brown staining:* × 100.)

a, horny layer of the epidermis.
b, rete Malpighii.
c, corium.
d, horny layer swollen up and infiltrated with leucocytes.
e, swollen cells of the rete Malpighii.
f, swollen epidermis infiltrated with cells.
g, degenerate epidermal cells, into which leucocytes have penetrated.
h, granular coagula.
i, swollen papilla infiltrated with cells.
k, corium infiltrated with cells and fibrin.
l, lymphatic vessel.
m, sweat-gland.

is formed (*lupus erythematosus discoides*). In other cases the disease advances not by the growth of old spots but by the continual development of the new ones (*lupus erythematosus disseminatus*).

The morbid process consists in an inflammation of the cutis, especially in the neighborhood of the sebaceous and sudoriparous glands

(KAPOSI and THIN). The epithelium of the glands multiplies, the epidermis is swollen, and scales and sometimes vesicles are formed on its surface. In the later stages both the epidermal and fibrous constituents of the skin become atrophied.

See HEBRA and KAPOSI (*Diseases of the skin* IV.), GEBER (*Viertelj. f. Derm. u. Syph.* III.), THIN (*Med. chir. Trans.* 1875), STROGANOW (*Cent. f. d. med. Wiss.* 48, 1877).

381. **Burns and blisters.** When the skin is exposed to the action of **heat** in such a way that the epidermis is killed, while the underlying cutis and its vessels are injured but not killed outright, blisters are formed on the surface; in other words, the skin reddened by congestive hyperæmia is raised into vesicles or blebs containing clear liquid. The changes through which such a blister may pass are various. Usually the lost epidermis is quickly replaced by regenerative growth under cover of the horny shell of the blister (Art. 374, Fig. 149). The exuded liquid disappears by evaporation, and if after a day or two the dry shell of epidermis be removed the denuded surface will be found completely covered with new epidermis, and the injury is indicated only by the bright red tint of the spot.

When irritant matters gain access to the denuded papillary surface, as may happen if the skin of the blister is prematurely removed, the healing process is notably delayed. The exudation of liquid and cells continues for some time longer, the deep-red surface secreting a more or less turbid liquid (catarrhal exudations). But presently this ceases and the epidermis is reproduced. This more protracted process of repair is to be looked for when the injury caused by the burn extends to the papillæ and deeper layers of the cutis.

The blisters caused by **cantharides** are of much the same character, but the swelling and solution of epidermis is usually less sudden and less extensive. Denucleated continuous masses are sometimes formed from the necrosed epidermal cells.

We may perhaps remind the student that burns may be of very different degrees of severity. It is sufficient for most purposes to distinguish three degrees. In the first there is merely erythematous reddening of the skin; in the second blisters are formed; in the third some portions of the fibrous structures are destroyed (Art. 389). Many transitional grades exist between these: for example, in burns of the second degree it often happens that not all of the epidermal layers become necrotic, but only the surface layers. Accordingly the general course of the process and the accompanying series of textural changes will vary in different cases. The solution of the epidermal cells in the exuded liquid is in fact seldom so complete or so general as might be inferred from the text, and the surviving cells may be strangely distorted and displaced (Art. 371). When the injury is very severe, so that inflammation of the denuded structures persists for some time, pus-corpuscles may be found not only in the surface strata, but also in the fibrous structures beneath.

382. **Miliaria crystallina** or **sudamina** are small watery vesicles

covered by a delicate film of epidermis, which sometimes appear in the course of puerperal fevers, typhoid, acute rheumatism, etc., and last for a few days. They occur chiefly on the trunk. In this as in other vesicular eruptions, the epidermal cells are partly dissolved, the solution being preceded by serous infiltration of the papillæ as well as of the epidermis. After a short time the epidermis is reproduced beneath the vesicle, whose contents are at first mainly liquid but afterwards contain cells. When a new horny layer is formed the contents are enclosed as it were between two shells. The cellular infiltration of the corium persists for some time, the lymphatics especially continuing to retain the extravasated cells with which they are filled.

383. **Herpes** is an acute affection running a typical course (KAPOSI) characterized by the formation of clusters of watery vesicles on certain parts or regions of the body, and passing through a definite cycle of stages within a short period of time.

The eruption first appears as a group of minute papular elevations of the skin, which rapidly become infiltrated with watery serum and become vesicles. This is the climax of the process: the vesicles last one to four days and then dry up into crusts. Beneath the crusts regenerative proliferation of the epidermis takes place, the lost tissue is thus made good, and the crusts are gradually loosened and cast off.

The vesicles of herpes take their rise in the deeper layers of the rete Malpighii; its cells swell up and become vacuolated (Art. 371), or become compressed and distorted as the exudation accumulates.

The contents of the vesicles consist of serum, fibrinous coagula, and pus corpuscles, the latter especially in the later stages. The papillæ are infiltrated more or less intensely with serous liquid and leucocytes, and occasionally hemorrhage takes place. Sometimes this may lead to the destruction a few of the papillæ, and then a scar is left after the eruption passes away.

Five forms of herpes are distinguished according to their seat and mode of origin.

(1) **Herpes zoster** (*zona* or shingles) is an eruption of vesicles clustered over the area supplied by a cutaneous nerve; it is almost always unilateral. The contents of the vesicles remain clear for three or four days, then they become turbid and purulent. Yellowish-brown crusts are formed as the vesicles dry up. Sometimes hemorrhage takes place into the vesicles.

BRIGHT (*Medical Cases* II. London 1831) suggested the connection of the eruption with disorder of a sentient nerve, and BÄRENSPRUNG (*Charité Annalen* IX., XI., *Brit. For. Med. Chir. Rev.* 1862) demonstrated the fact, and showed that simultaneous changes sometimes occur in the spinal ganglia and Gasserian ganglion. RAYER, WEIDNER, E. WAGNER, CHARCOT, KAPOSI, BOHN, E. LESSER, NEUMANN, and others have verified the observation, and have shown that affections of the cord and of the peripheral nerves may give rise to vesicular eruptions. The nerve-affections referred to are partly primary, partly secondary to some affection in their neighborhood or to some mechanical injury. The morbid

change is generally of the nature of inflammation or hæmorrhage, in consequence of which nerve-fibres and ganglion cells are injured or destroyed.

References: KAPOSI, *Wien. med. Woch.* 1874, 1875, 1877, *Lond. Med. Record* 1876; BOHN, *Jahrb. f. Kinderheilk.* II. (1869); CHARCOT *Diseases of the Nervous System* vol. I. (New Syd. Soc.) 1877; HAIGHT, *Sitzungsber. d. k. Wien. Akad.* 1868; WEIDNER, *Berl. klin. Woch.* 7, 1870; WAGNER, *Arch. d. Heilk.* XI.; WYSS; *ibid.* XII.; E. LESSER, *Virch. Arch.* vol. 86; NEUMANN, *Lehrb. d. Hautkrank.* Vienna 1880; ROSS, *Diseases of the Nervous System* I. London 1883.

(2) **Herpes labialis** (*facialis*) is an acute eruption of vesicles on the lips or around the mouth and nostrils. The vesicles last two or three days and dry up under a crust, without scarring. Its cause is unknown, but it is very often observed in connection with pneumonia and intermittent fever, and more rarely in typhoid.

(3) **Herpes progenitalis** (*præputialis*) affects the penis, clitoris, or labia; its course is similar to that of herpes labialis.

(4) **Herpes iris** and **herpes circinatus** are according to KAPOSI the same as erythema iris and circinatus (Art. 367). The vesicles occur on the back of the hands or feet and form separate or concentric circles; they fade after eight or ten days.

(5) **Herpes tonsurans vesiculosis** is a special form of tinea (herpes) tonsurans (Art. 411), an affection caused by a vegetable parasite. Circles of vesicles of various sizes are formed by successive marginal crops starting from a centre; the older vesicles dry up as new ones develop.

384. **Pemphigus** is an eruption characterized by the formation of vesicles and blebs varying in size from that of a small pea to that of a goose's egg. The vesicles are usually preceded by red spots and wheals, but they may rise on what seems unaltered skin. The contents are at first clear and watery, or it may be slightly blood-stained; but afterwards they become turbid and purulent. The exudation at length dries up and crusts are formed, under which the lost epidermis is reproduced (*pemphigus vulgaris*). In other cases the regeneration of the epidermis does not at once take place, and the separation of the epidermal layer covering the bleb extends, so that at length a large area of the corium may be denuded (*pemphigus foliaceous*). When the skin of the bleb is removed the exposed surface is red and moist until a crust is formed from the superficial exudations. In such cases the corium is always more or less infiltrated, and sometimes it may in part become necrotic and break down (*pemphigus malignus* and *diphtheriticus*). Granulations are then produced, but they too are very liable to necrosis (KAPOSI).

The smaller vesicles are usually loculated, the large blebs are single. The under-surface of the epidermal shell of the bleb is often beset with epithelial projections, which have been pulled out of the tubes of the hair-follicles.

Four chief forms of pemphigus are distinguished according to their clinical characters (KAPOSI).

(1) **Pemphigus acutus** is an acute affection manifested by an eruption of scattered blebs, with or without fever. The blebs last a few hours and then dry up into crusts. When these fall off the corium is covered with new epidermis, and the attack is at an end.

(2) **Pemphigus chronicus vulgaris** is characterized by the formation of large tense blebs, accompanied by a certain amount of fever. The eruption take place by successive crops. According to the mode in which the blebs are grouped, we have *pemphigus disseminatus* (scattered irregularly), *pemphigus confertus* (closely aggregated), *pemphigus circinatus* (in circles), and *pemphigus gyratus* or *serpiginosus* (in convoluted or undulating lines). The disease lasts from two to six months, and sometimes ends fatally. GIBLER (*Gaz. de Paris* 1881) asserts that febrile pemphigus is a bacterial affection.

(3) **Pemphigus foliaceus** is the severest form of the disease. It is distinguished by its progressive character and the imperfect way in which the lost epidermis is reproduced. After months or years the entire surface of the body may be affected. The skin is then in places brown and parchment-like, in others red and weeping; the spots are covered with crusts and fissured in various ways.

(4) **Pemphigus syphiliticus** is considered in Art. 386.

385. **Eczema** is a skin-disease which may be acute or chronic; the eruption consists of papules, vesicles, or pustules; the skin is more or less reddened and swollen, and desquamates, or "weeps," or is covered with large continuous scabs. Eczema is set up by external irritation. When the irritation is slight the eruption consists of small papules, and thus *eczema papulosum* is the mildest variety. Somewhat more intense irritation causes small vesicles to arise, and we have *eczema vesiculosum;* when the vesicles dry up they are cast off as scales. If the irritation is still more intense or the skin highly susceptible, a considerable area becomes painfully red and swollen (*eczema erythematosum*). On this vesicles arise, which are at first clear but soon become purulent (*eczema pustulosum*). When the upper shell of the vesicles is removed (as by scratching) the exposed surface pours out liquid and is said to 'weep' (*eczema madidans*). The epidermic surface deprived of its horny layer by desquamation or otherwise has often a deep-red tint (*eczema rubrum*). Crusts are formed by the evaporation of the sero-purulent exudation poured out on the surface (*eczema crustosum*), and pus sometimes gathers beneath the crusts (*eczema impetiginosum*). In other instances new epidermis is formed beneath the crusts; when the crusts are cast off the surface then looks red and brawny and scales are freely shed (*eczema squamosum*). As the disease disappears the skin gradually recovers its normal appearance, though some slight pigmentation often remains (KAPOSI). An eczematous eruption consisting of pustules of the size of a small pea, and drying into scabs without rupturing, is often described as **impetigo.** Much larger pustules, seated on an inflamed and reddened base and drying into brown scabs, constitute **ecthyma. Impetigo contagiosa** is a contagious eczematous eruption (TILBURY FOX, *Brit. Med. Journ.* 1864; UNNA, *Viertelj. f. Derm. u. Syph.* VII.). It chiefly attacks ill-fed or weakly children, and affects the head and limbs: vesicles as big as a cherry-stone arise on a reddened base, and presently dry up into yellow crusts.

The inflammatory process in eczema is often chronic, and the skin is

then beset with vesicles, pustules, scales, and scabs, all at the same time.

The textural changes in the cutis consist of serous and cellular infiltrations of the fibrous tissue. The cellular infiltration is especially dense in the pustular and impetiginous varieties, and the subcutaneous tissues are often infiltrated in the same way.

As regards the epidermis, some of the cells of its mucous layer perish in the vesicular stage, and some are compressed and stretched into fusiform or other shapes. The liquid exudation contains numbers of leucocytes, which are found not only in the vesicles but also scattered among the unaltered epidermal cells, and even in their interior. In many cases the epidermis perishes outright, and even the papillæ may be destroyed when the inflammation becomes suppurative (*eczema impetiginosum*).

The after-effects of eczema are various. Slighter forms leave no trace behind, the skin being restored *ad integrum*. If the papillæ have been injured or destroyed they are not replaced, and a cicatrix is produced. Chronic eczema gives rise to pigmentation, and to hypertrophy of both epidermis and corium: when the hypertrophy is great the skin appears thick and dense as in elephantiasis; when the papillæ are likewise enlarged the surface becomes warty and tuberculated. Hypertrophy of the epidermis being generally accompanied by the formation of plates, scales, and flakes, an appearance recalling that of elephantiasis combined with ichthyosis is produced (Arts. 394, 396 and 413). So long as the inflammation persists the hypertrophied fibrous tissue is thickly beset with clusters of young leucocytes. They are occasionally aggregated into nodules containing giant-cells.

386. The **pustular syphilide** follows upon the papular form (Art. 379) by the development of pustules above the papules. Small pustular and large pustular varieties may be distinguished. The latter are often described as syphilitic variola, acne, or impetigo. The pustules are surrounded by a red infiltrated raised border. When the papules and pustules grow to any considerable size the eruption is described as *pemphigus syphiliticus*, and when these harden into crusts they form *rupia syphilitica*.

The **syphilitic pemphigus of infants** (Fig. 152) calls for special mention. It occurs chiefly on the limbs of infants suffering from congenital syphilis, and may appear at birth or in the first few weeks of life. The vesicles arise in the same way as other inflammatory vesicles, by the destruction and solution of the cells of the mucous layer. But the affection is distinguished by the fact that the floor of the vesicles and blebs is occupied by large-celled vascular granulation-tissue (*i*) developed from the cutis and papillæ.

Infantile syphilitic pemphigus is not strictly one of the group of affections we are now discussing. It differs from them inasmuch as it includes the formation not only of an inflammatory exudation, but also of new-formed vascular granu-

lation-tissue. It has been mentioned in this place because its appearance to the naked eye so closely resembles that of the other phlyctænoses.

387. **Small-pox** or *variola* is a general febrile disease characterized by the eruption of papules, vesicles, and pustules, and caused by the the infection of the system with variolous poison. After a certain inter- from the time of infection the skin becomes suddenly beset with hard red papules of the size of a pin-head, surrounded by a red areola. Some of the papules enlarge and change into clear vesicles most of which are umbilicated, *i. e.* depressed in the centre. In two or three days the contents of the vesicles become turbid, and the vesicle becomes a pustule. At the same time the umbilication usually disappears, and a zone of intense hyperæmia is formed around the pustule. In three or four days it dries to a brownish scab, and this in a few days more falls off, leaving

FIG. 152. INFANTILE SYPHILITIC PEMPHIGUS.

(*Section through the margin of a vesicle ; hæmatoxylin staining :* × 200.)

a, normal horny layer of the epidermis.
b, normal rete Malpighii.
c, corium.
d, swollen and desquamating horny layer.
e, swollen cells of the rete.
f, vacuolated epidermal cells.
g, remnants of the rete compressed by the contents of the vesicle.
h, vesicle produced by the destruction of the deeper layers of the rete.
i, granulations arising from the cutis and papillæ.

behind a slightly pitted spot, which may be red or brown or white in color; in a short time the spot also disappears.

Frequently however the course of the disease is much less favorable. Some of the pustules do not heal up without cicatrization, so that scar-like pits are left which at first are dark-red, but afterwards are white and permanent. This is especially the case when hæmorrhage takes place into the pustule, or when the eruption is so copious that the pustules run

together (confluent small-pox). The skin appears rough and tuberculated and is much swollen. When the cap of the pustule is forced off by the accumulating pus within, the suppurating corium is laid bare, and parts of it may become necrosed or gangrenous. The affected spots have a dirty gray or black tinge.

The variety distinguished as hæmorrhagic or black small-pox (*variola hæmorrhagica* or *purpura variolosa*, Art. 361) is remarkable for the dark-red color which overspreads the entire surface of the body as the fever sets in. Patches of hæmorrhage appear, and soon enlarge in an astonishing way. Death ensues in a few days, and on post-mortem examination hæmorrhages are found in various internal organs. In other cases a multitude of small hard papules appear on the skin, which is intensely swollen but not necessarily discolored; hæmorrhagic patches follow in one or two days, and speedily coalesce into larger ones. This form also is apt to end fatally.

388. The histological changes observed during the evolution of the variolous pustule have already been partially treated in Arts. 371 and 372. The first change is the swelling up of the cells of the mucous layer of the epidermis immediately over the tips of the papillæ. WEIGERT has shown that the swollen cells are transformed into pale denucleated masses resembling coagula. This is followed by complete necrosis and solution of the affected cells in the exudation which at this stage is poured out from the papillary vessels, while the degenerative swelling and change extend on all sides. Only small portions of the epidermal tissue withstand solution, and these are chiefly cell-membranes, or degenerate denucleated or sometimes nucleated masses representing coagulated cells; these are stretched and compressed by the accumulating exudation into bands and threads and partial septa crossing the excavations in the epidermis.

Thus at the climax of the process the pock or vesicle consists of a cavity traversed by shreds of membrane and fibres and distorted cells (Fig. 153 *f*) covered at its highest part by the horny layer only (*i*), but towards its margins by some of the surface layers of the epidermis as well. The floor of the cavity is formed of remnants of the inter-papillary portion of the rete Malpighii (*g*), and in part of denuded papillæ (*h*). The papillæ and the upper layers of the cutis are swollen and beset with leucocytes; and the liquid contents of the vesicle already contain numerous free cells and pus-corpuscles (f_1).

As the pock becomes a pustule the number of pus-corpuscles which pass into the cavity from the papillary vessels increases, and the shreds and septa break down. The pustule dries into a crust, the infiltrated cells are re-absorbed, and repair begins under the crust starting from the margins where the epidermal cells are uninjured.

A pock like that in Fig. 153 leaves no scar behind it, as nothing is destroyed which is not completely replaced. When the inflammation is

more intense the process of healing is different, inasmuch as the papillæ themselves break down or suppurate. Complete repair is no longer possible, and the site of the pock is marked by a cicatricial depression (**pock-mark** or **pit**). A pock in which the papillary layer suppurates is sometimes called a diphtheritic pock.

Recent researches have made it probable that small-pox is due to the invasion of a specific bacterium (Art. 204). WEIGERT (*Anat. Beiträge zur Lehre von den Pocken* Breslau 1874) thinks the first effect of the virus is to produce necrosis of the epidermal cells, and that all the other phenomena are due to the reaction set up in consequence of this necrosis. This view seems somewhat one-sided. Even if we grant that the virus has a destructive action on the epidermis, there appears no reason to doubt that it has also an injurious effect upon the vessels, producing in their walls the alterations which lead to the phenomena of inflammation. The early appearance of the exudation is in favor of such an inference, and the epidermal changes above described follow naturally upon the exudation.

UNNA'S statement (*Virch. Arch.* vol. 69)--that the pock is seated on the deep-

FIG. 153. SECTION OF A VARIOLOUS VESICLE BECOMING PUSTULAR.

(*Injected preparation, stained with hæmatoxylin:* × 25.)

a, horny layer.
b, mucous layer.
d, cutis.
e, vesicle.
f, cavity of the vesicle.
f_1, pus corpuscles.
g, fragments of epidermal cells interspersed with pus-corpuscles.
h papilla infiltrated with leucocytes.
i, umbilication over the thinnest part of the cap of the vesicle.
i_1, margins of the vesicle, where the cap consists of several layers of epidermis.

est or basal stratum (*stratum lucidum*) of the horny layer—ZIEGLER has not been able to confirm: but their researches were not carried out on the same part of the body. ZIEGLER found that the vesicles were seated above the rete Malpighii only in cases where a certain amount of regenerative epidermal proliferation had taken place on the floor of the cavity. The mode in which this would tend to raise the pock towards the surface has been pointed out in Art. 374 (Fig. 149). Fig. 153 shows how the regenerative growth of the epidermis near the papilla *b* on the left margin tends to thrust the vesicle upwards.

The umbilication of the vesicle has given rise to some controversy. RINDFLEISCH (*Pathological Histology* vol. I. London 1872) and HEBRA (*Diseases of the*

skin I.) think the roof of the cavity is held down by the persistence of the tubes of the hair-follicles and sweat-glands. AUSPITZ and BASCH (*Virch. Arch.* vol. 28) maintain that the distention of the middle parts by the exudation does not keep pace with the elevation of the margins by infiltrative swelling. WEIGERT states that the shreds and partial septa which cross the cavity suffice to hold down the cap in its centre. Probably both the factors emphasized by the latter authors come into play.

The vesicles of **vaccinia**, produced by vaccination, have the same structure and pass through the same stages as the variolous vesicle. The eruption does not tend to become general.

Chicken-pox or *varicella* is a febrile disease characterized by eruptions of vesicles in successive crops, and caused by a specific contagion. The vesicles start in rosy slightly raised spots, which speedily become infiltrated and distended with a clear liquid; they are usually surrounded by a reddened areola. They may be as large as a split pea, and are sometimes umbilicated. In a day or two their contents become turbid, and then they rupture or dry up into dark adherent scabs. As the scab separates a reddish stain is left, which usually disappears in a few days.

c. *Eruptions ending in necrosis, suppuratiom, ulceration, or granulation.*

389. The affections of the skin which we have hitherto discussed have been inflammations either of a transient kind ending in complete recovery, or such as produce sensible changes of structure but not complete destruction of the skin. Only as a rare exception do they give rise to loss of substance calling for repair by granulations and cicatricial tissue.

The processes now to be described are inflammations which issue in suppuration or necrosis of portions of the integument, and to which the development of granulations and cicatricial tissue is the ordinary and typical sequel.

The injurious agencies which induce the skin-affections of this group are in part the same as those concerned in the less grave affections; but much more frequently they belong to a special and peculiar class, namely the class of specific contagia or infective poisons. The differences in the intensity of the inflammatory processes set up are in part due to differences of predisposition in the patient, and in part to differences in the intensity of the injury or the virulence of the poison. A typical example of the first is afforded by small-pox, which in 'protected' patients, that is in patients with but slight predisposition to the disease, runs a mild course without any marked after-effects: in unprotected or predisposed patients the inflammation set up leads to extensive and permanent destruction of the skin. An obvious example of the increase of the effect with increase in the intensity of the injurious agency is afforded by burns of the third degree (Art. 381). In such burns the epidermis, the cutis, and perhaps the subcutaneous tissue are destroyed or killed: intense inflammation then ensues, by which the dead tissue is gradually separated from the living. Granulations are developed in the

form of fleshy upgrowths from the floor of the wound, and from them scar-tissue is elaborated, which may become more or less completely covered over with new epidermis growing from its margins. The scar is smooth and devoid of any regular papillæ; and it soon becomes vascular and therefore red in tint. After a time however many of the vessels shrivel up, the tissue becomes pale, contracts, and forms a white tense puckered cicatrix. When the loss of substance caused by the original burn is extensive, the contraction of the scar may be so great that the function of the part (a limb, for example) may be seriously interfered with.

The general effects of high temperatures are also produced by much lower temperatures, the difference being rather one of extent and degree than of kind. The inflammation induced may be slight and transient, and may lead to necrosis of small portions of the integument. The necrosis is followed by a definite inflammation by which the dead tissue is separated, and then granulations and cicatricial tissue are formed.

Many corrosive chemicals act like high temperatures, and the effects of mechanical injury are often graduated in much the same fashion according to the intensity of the injury. Thus cuts and wounds which heal up without loss of substance may be distinguished from those in which deficiency or destruction of tissue requires to be made good by the development of a bulky cicatrix (Arts. 106–111).

It need hardly be said that the above account by no means exhausts the ways in which external injury may affect the skin. In speaking of temperatures we have had in mind only the direct effects of short exposure to somewhat high and somewhat low temperatures. But it is well known that exposure to temperatures differing little from the normal may produce notable effects on the skin if it is long continued or frequently repeated. Repeated cooling of the feet and hands gives rise in susceptible patients to what are called **chilblains** (*perniones*), that is to livid swellings of the skin due to inflammatory exudation and often passing into suppuration. Similar remarks apply to many other varieties of injurious agency.

390. Of the cutaneous inflammations leading to suppuration and necrosis which have received special names (on account of their peculiar course or mode of origin) we must in the first place mention two—namely phlegmon or phlegmonous inflammation, and malignant pustule.

Phlegmonous inflammation or cellulitis is due to the invasion of a micrococcus (Art. 204) which enters the cutaneous tissues at some wounded spot. In the living patient or after death the affected skin is intensely reddened and swollen. The swelling is due to an abundant infiltration of sero-purulent, fibrino-purulent, or simply purulent liquid in the spaces of the cutaneous and especially the subcutaneous tissues. In recent cases the micrococci are also to be found in these tissue.

The violent inflammation set up and the consequent disturbance of the circulation lead to the death of the tissues over a greater or smaller

area, and extensive suppuration results. Collections of pus, or **phlegmonous abscesses,** are thus formed in the skin and subcutaneous tissue, and they contain shreds and fragments of necrosed tissue.

Phlegmonous inflammation chiefly occurs in the limbs. A special variety attacks the phalanges of the fingers and leads to an extremely painful swelling with partial suppuration: it is called **whitlow** (*panaritium* or *paronychia tendinosa*).

Malignant pustule or **specific anthrax** is an affection caused by the invasion of the *Bacillus anthracis* (Arts. 186, 206). It almost always attacks parts that are habitually uncovered, and especially the face. In the skin it begins with redness and swelling which spread from the site of infection. This last soon becomes gangrenous and is often surrounded by a ring of dark or livid blebs; a small umbilicated bleb sometimes covers the site itself. Now and then large tumor-like swellings arise, whose general configuration is that of a magnified pock (Koch), the umbilicated summit being dark-colored and the margin formed by a yellowish circular élevation. When the blackened epidermal cap is cast off a clear liquid is poured out from the diseased tissue: no pus is ever formed. The swelling is due to sero-fibrinous and cellular exudation. The neighboring lymphatics and glands speedily become affected.

An affection of the skin resembling that due to anthrax may be caused by an invasion of micrococci, the infection starting as in anthrax from some small surface wound. Occasionally it may be caused by the sting of an infected insect. The intensity and extent of the swelling is usually greater than in anthrax, and gangrene sets in around the site of infection. After the necrosed tissue is cast off the wound may cicatrize; but occasionally fatal blood-poisoning is induced.

Another allied form, also due to bacteria, is the so-called **hospital gangrene.** It is a traumatic infective disease which may attack any wound, but is most apt to occur in connection with minor surface wounds like those due to cupping or leech-bites. The micrococcus which causes it is specific. The infected wound assumes a dirty yellow or gray tint and becomes gangrenous. When the wound contains granulations they become discolored and change into a yellowish creamy pulp which speedily breaks down and liquefies, and the wound secretes a putrid serous or sanious liquid.

Gangrenous bed-sores are not to be confounded with specific hospital gangrene. They occur in emaciated patients with feeble circulation. Very slight pressure is therefore enough to cause necrosis of the skin. The affected parts are livid or black, and under the influence of ordinary septic organisms become putrid and break down. The commonest sites of such bed-sores are over the sacrum, great trochanter, and heel. They often extend through the skin to the tissues lying beneath.

Cadaveric poison (so-called) is apt to induce grave inflammation leading to suppuration and necrosis. The affection normally continues as a

local one, painful redness and swelling are set up round the infected spot, and these are followed by suppuration. In other instances the inflammation becomes diffuse and phlegmonous, or lymphangitis is set up in connection with the local affection (Art. 314). When it becomes chronic, hyperplasia of the skin with enlargement of the papillæ and thickening of the epidermis is produced. The knotty and tuberculated projections thus formed are spoken of as necrogenic or **'dissecting-room' warts.**

391. **Ulcers of the skin.** A cutaneous ulcer is an open wound extending to the cutis, the tissues of the floor and margins being infiltrated with inflammatory products and undergoing progressive molecular disintegration. Many ulcers have granulations covering their floors, which however show no great tendency to cicatrization.

Ulcers vary greatly in their outward appearance. Usually the floor is covered with a grayish film consisting of pus and necrotic tissue. The surface of the floor may be smooth, or nodulated, or irregularly excavated. The edges may be raised or undermined, or abrupt and sharply cut or sloping; they may be regularly rounded or sinuous or serrated. The surrounding parts may be intensely red and swollen or altogether unaltered, they may be hard and densely infiltrated or soft and œdematous. The liquid exuded from the surface may be scanty or abundant, limpid or thick and creamy. Crusts or gum-like pellicles are often formed as the exudation dries, or the ulcer may be covered over with a dirty-looking diphtheritic film.

An ulcer is generally the result of necrosis befalling a portion of skin which has previously been infiltrated with inflammatory products. The progressive disintegration of tissue, in consequence of which the ulcer grows in size, depends either on something in the nature of the tissue, or on the character of the injurious agent which sets up the inflammation; the latter being the more frequent factor.

The following varieties are distinguished by their special mode of origin.

(1) **The varicose ulcer.** This is primarily due to engorgement and dilatation of cutaneous veins and consequent œdematous infiltration of the tissues: comparatively slight injury is then enough to induce abundant cellular infiltration, and this passes into suppuration and necrosis. The ulcer granulates readily, but does not heal so long as the exciting cause persists. Not only does it fail to 'skin over,' but it often continues to extend over the surface and may reach an enormous size. The surrounding fibrous tissues become thickened in consequence of the long-standing œdema and the formation of new tissue. The granulations have no special characters, and may be scanty or exuberant ('proud flesh').

The epidermis bordering on the granulations often thrusts in prolongations and off-shoots into the midst of them, but does not advance

regularly over their surface. The tissues around and underlying the ulcer usually show signs of persistent engorgement, such as cyanotic discoloration, desquamation of the epidermis, dilated veins, œdematous infiltration, etc. The leg and foot are the commonest sites.

(2) **The soft chancre** or **chancroid.** This is a contagious localized venereal affection, beginning some twenty-four hours after infection as a vesicle or pustule, and rapidly becoming an ulcer with a yellowish base and reddened border. It grows by progressive molecular death of the border-tissue. The edges and base are at first thickly infiltrated with cells, and these as they near the surface pass through successive stages of degeneration and decay, and at length form a layer of structureless detritus. A soft chancre may give rise to lymphangitis and bubo, but not to syphilitic disease.

(3) **The hard chancre.** When a patient is infected simultaneously with the venereal poison which gives rise to soft chancre and with syphilis, the base of the soft chancre becomes indurated about the third or fourth week after infection. The soft chancre is thus converted into a hard chancre. If the soft chancre has healed quickly the characteristic induration appears in the cicatrix.

When syphilis is communicated without the simple venereal poison the first thing seen is a papule, which appears in the third or fourth week after infection. The papule extends laterally, and in eight or ten days becomes scaly or breaks down into an ulcer secreting a small quantity of serous or slightly puriform liquid, which presently dries up into a crust or scab. At the same time the base becomes indurated and forms a definite cartilaginous or parchment-like disc under the skin. This indurated sore is described as the initial sclerosis of syphilis, or the true **Hunterian chancre.** It is due to a dense cellular infiltration of the integument, without any very special histological features. CORNIL's statement (*Leçons sur la Syphilis* Paris 1879 , *Syphilis* London 1882) that the indurated tissue is infiltrated to an extreme degree is correct; but infiltrations quite as intense are met with in other forms of granulomatous ulcer—notably in tuberculous affections. The reason why the infiltrated tissue is so hard seems to be—that the fibres of the connective tissue persist unchanged for a considerable time, while in the soft sore they very speedily break down.

The infiltrated cells are at first uniformly small, but in the later stages they are larger, epithelioid, and often multinuclear (Art. 128). The induration sooner or later disappears, the parchment-like form being the first to go. If no ulcer has been formed, a scar-like unpigmented spot is left behind; if an ulcer has been formed a regular scar takes its place.

(4) **The gummatous ulcer.** Gummata of the skin (the papular or tubercular syphilide) may give rise to a second variety of syphilitic ulceration. Nodes of various sizes are formed in the skin or subcutaneous tissue, and are either reabsorbed or break down and ulcerate, the ulcers

having indurated bases and edges, and often spreading over a wide extent. When the secretion as it dries forms a thick raised crust over the sore, the affection is described as syphilitic **rupia.** It is characterized by its infiltrated border. For the structure of gummata see Arts. 129 and 130.

(5) **The scrofulous ulcer.** This begins with the formation of cellular nodes or nodules which appear in the skin or subcutaneous tissue. They are simply foci of cellular infiltration, and greatly resemble gummata in the initial stage. They occur chiefly in children. As they break down they give rise to indefinite ulcers with soft œdematous borders, which bleed very readily and secrete a creamy pus. Similar ulcers are formed when subcutaneous lymphatic glands break down and suppurate.

(6) **The true tuberculous ulcer** of the skin is very rare. In diagnosing it we have to depend on the presence of undoubted tubercles in the base of the ulcer or in the surrounding tissue.

We mentioned in Art. 206 that KLEBS had discovered small bacilli in excised portions of hard chancres. AUFRECHT on the other hand found micrococci in syphilitic mucous patches (*Cent. f. d. med. Wiss.* 13, 1881). BEKMANN (*New York Med. Journ.* Dec. 1880) describes micrococci and bacteria in the lymphatics around the initial sclerosis. BIRCH-HIRSCHFELD has recently announced (*Cent. f. d. med. Wiss.* 44, 1882) that not only the primary sore but also the gummatous nodes contain small bacilli (1 microm. in length), some lying free in the tissues, others enclosed in cells. He considers these to be the vehicle of the syphilitic contagion.

Tuberculosis of the skin appears in the form of ulcers, and of nodes and nodular clusters of cells. It is very questionable whether all cellular nodes and ulcers containing tubercles are produced by the action of the tuberculous virus. In this connection it must be remembered that lupous granulations also contain tubercular aggregations of cells. On cutaneous tuberculosis see KÖSTER (*Cent. f. d. med. Wiss.* 1873); FRIEDLÄNDER (*Samm. klin. Votrâge* 64, *Virch. Arch.* vol. 60); BIZZOZERO (*Giorn. d. acad. di med. e. chir.* 1874); BRODOWSKI (*Virch. Arch.* vol. 63); CHIARI (*Wiener med. Jahrb.* 1877, *Viertelj. f Derm. u. Syph.* VI.); HALL (*Ueb. Tuberculose d. Haut* In. Diss. Bonn 1879).

392. Granulation-tissue may (as we have seen) be produced in many ways and as the result of very various processes. All inflammations which involve destruction of tissue may give rise to it in the process of healing and cicatrization. Sometimes however the granulations become as it were redundant, and do not pass into the stage of cicatrization. In this way they may take on a quasi-independent character and form tumor-like aggregations of considerable size, the so-called granulomata. Non-specific inflammations, such as eczema, may be followed by such granulomatous overgrowth; but it is in general associated with certain specific infections, and the growths are therefore referred to as the infective granulomata. We have already partially considered them in Arts. 128–135, and the tubercular syphilide or gummatous ulcer of the skin has been mentioned in Art. 391. Here therefore there is little further to say about the group in general.

Lupus is a skin-affection characterized by the formation in the sub-

epidermal layers of nodular patches of granulation-tissue (Fig. 154 *d*). Sometimes these nodules have the structure of the tubercles of tuberculosis, sometimes they consist entirely of small leucocytes with occasional capillaries (*d*). The eruption of the nodules is accompanied by diffuse cellular infiltration of the cutis and papillæ (*c*), and by the formation of strings of cells (*f*) running with the lymphatics. Redundant multiplication of the epidermal cells is often induced (*h*), and epidermal growths penetrate the deeper layers of the skin; when they reach a certain size they remind one of the cellular ingrowths of carcinoma. The surface layers may moreover be here and there swollen, or vacuolated, or in process of desquamation.

FIG. 154. PATCH OF LUPUS VULGARIS.

(*Carmine staining:* × 25.)

a, normal epidermis.
b, normal cutis with sweat-gland (*i*).
c, focus of lupus-tissue.
d, vascular nodule surrounded by diffuse cellular infiltration.
e, non-vascular nodule.
f, strings of cells.
g, lupous ulcer.
h, proliferous epidermis.
i, sweat-gland.

The hair-follicles and sebaceous glands are also affected, and the hair perishes in consequence. The glands cease to secrete sebum, and may become greatly distended and enlarged by the accumulation in their ducts of epithelial cells. Sometimes the cellular infiltration is most dense in the immediate neighborhood of the sebaceus glands.

The infiltrated tissue generally becomes necrotic, softens, and breaks through the epidermis (*g*); in this way lupous ulcers are formed which by gradual advance may involve a very large extent of the surface. In some cases however the nodules are re-absorbed without ulceration.

Some of the extravasated cells are utilized in forming new fibrous tissue, and the papillæ may in this way become notably enlarged, the skin as a whole may thicken, and at length the ulcerated tissue may be re-

placed by a cicatrix. After a time the new tissue contracts and a puckered scar is left.

Lupus first appears as a local eruption of small bright red or brownish spots (KAPOSI); after a time nodular prominences can be seen and felt under the skin, and the nodules coalesce so as to form larger nodes and tubercles (*lupus tumidus*). In a few weeks retrogressive changes set in: if the nodules are absorbed the epidermis becomes wrinkled and desquamates (*lupus exfoliativus*) leaving a scar-like patch behind; if they soften and break through the surface (*lupus exulcerans* or *exedens*) rounded ulcers are formed, with soft and reddened margins and red granulating floors, secreting pus and often becoming crusted over. The ulcers may heal by scarring and skinning, or warty growths may appear on the floor (*lupus verrucosus* or *papillaris*). If the nodules are at the outset irregularly scattered the affection is described as *lupus disseminatus*, if they are arranged in sinuous lines as *lupus serpiginosus*.

Lupus most commonly attacks the nose, but it very often occurs elsewhere on the face, in the neck, ears, mouth, nostrils, pharynx, larynx, and on the limbs, rarely on the trunk. The successive ulceration and cicatrization of the skin may in the course of years give rise to very remarkable deformity and disfigurement.

Leprosy has already been treated in Art. 131. The skin in this disease may be covered with flattened or nodular patches of cellular infiltration, which are red, brown, or white on the surface, and end either in desquamation or ulceration; the leprous patches and sores contain the specific *Bacillus lepræ* (Art. 206). According to VON RECKLINGHAUSEN the separate nodes and tuberosities develop chiefly around the cutaneous nerves. The ulcers formed by the disintegration of the nodes may become very deep and wide, and lead to the separation and loss of portions of the limbs (*lepra mutilans*). In *lepra maculosa* the skin is disfigured by diffuse pigmentations interspersed with streaks and patches of white.

References on leprosy:—Arts. 131, 206; BEHREND, *Schmidt's Jahrbücher* vol. 192 (a full summary of recent work); KAPOSI, *Hebra's Diseases of the skin* IV.; HILLIS, *Leprosy in British Guiana* London 1881; DUHRING, *Diseases of the skin* 1882; DAMSCH, *Virch. Arch.* vol. 92.

On lupus see HEBRA and KAPOSI, *Diseases of the skin* vol. IV.; VIRCHOW, *Die krankhaften Geschwülste;* AUSPITZ, *Wien. med. Jahrb.* 1864; LANG, *Vierteljahrs. f. Derm. u. Syph.* I., II.; KAPOSI, *ibid.* VI.; JARISCH, *ibid.* VII.; FRIEDLÄNDER, *Virch. Arch.* vol. 60; THOMA, *ibid.* vol. 65; THIN, *Med. chir. Trans.* LXII. (1879).

CHAPTER XXXIX.

INFLAMMATORY HYPERTROPHIES OF THE SKIN.

393. The inflammatory processes discussed in the last few Articles have this in common—that the formation of new tissue is inconsiderable, and in general little more than is necessary to make good the tissue which is lost. Even the granulomatous affections usually end in disintegration and ulceration, in the course of which the new granulation-tissue perishes. But we pointed out one or two exceptions to this rule, as for instance under eczema (Arts. 385, 392) and necrogenic pustule (Art. 390), in which chronic inflammation resulted in hyperplasia of the skin.

The **hyperplasia** may extend to the epidermal structures as well as to the fibrous elements. The excessive production of epidermal cells may be manifested simply by increased desquamation, or by thickening of one or more of the epidermal strata. Hyperplasia of the fibrous strata always involves an increase of their thickness over a more or less extensive area. When the papillæ are the structures most affected, they increase chiefly in length and often become subdivided as they grow, giving rise to unevennesses of the surface, which may be slight and wide-spread or aggregated into tumor-like masses.

The new tissue, while still recent, contains abundance of cells, and is in fact not far removed from granulation-tissue: in more advanced stages it contains fewer cells and is densely fibrous and scar-like. Both types may coexist in the same case.

394. When a part is continually exposed to slight mechanical irritation inducing often-repeated hyperæmia or slight inflammation, the epidermis may at length become hypertrophied. If the horny layer is chiefly involved, and callous or horny growths result, they are described as **callosities** (*tylomata*). They are commonest on the hands and feet.

When the callous thickening extends inwards and presses on the papillæ so as to lead to their atrophy, we have what is called a **corn** (*clavus*). The constant irritation of the papillary layer thus caused, especially when associated with external friction or pressure, induces more or less intense inflammation, and this occasionally passes into suppuration.

Sometimes the hypertrophy takes the form not of flattened or discoid thickening but of a horn-like protuberance (*cornu cutaneum*), which

may reach to a considerable size. The base usually includes a few enlarged and vascular papillæ.

Inflammatory warts are essentially of the same nature as the hypertrophies just described, though their appearance is very different. They are the result of long-continued irritation of a special kind. One of the commonest forms is that known as the **venereal wart** or cauliflower excrescence (*condyloma acuminatum*). This is usually seated on some part of the external genitals or around the anus; the special irritation which induces it is that caused by urethral discharges, chancrous pus, decomposed preputial or vaginal secretions, etc. The papillæ and the upper strata of the rete Malpighii become hypertrophied; the former (Fig. 155 *a*) become elongated and branched, and their blood-vessels are enlarged. The fibrous tissue on which they stand often becomes tumid at the same time, while the epidermal layers become thickened and hypertrophied, and so may cover over some of the irregularities caused

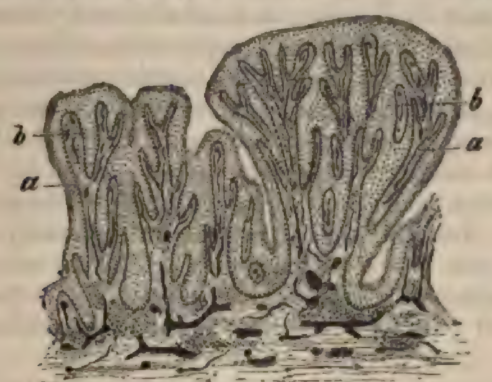


FIG. 155. VENEREAL WART.
(*Injected preparation, stained with hæmatoxylin:* × 20.)
a, enlarged and branched papilla. *b*, thickened epidermis.

by the branching of the papillæ. But many of these remain and are markedly exaggerated, so that the entire growth takes on a typically papillomatous appearance.

These warts are often very numerous and crowded together at one spot. Though small and inconspicuous at first they may grow to a remarkable size, and look like heads of cauliflowers. The papillæ as they grow tend more and more to subdivide; they are composed essentially of vascular fibrous tissue, but they always contain a number of leucocytes, and the base on which they stand is always more or less infiltrated. The lymphatics in the neighborhood may be extensively inflamed, as appears by the accumulation of cells within and around them.

Inflammatory papillomata may in like manner grow from the floor of an ulcer, especially such as occurs in connection with chronic impetiginous eczema (Art. 385). They may cover a wide area and give rise to diffuse

warty thickening of the skin (Art. 395). They usually possess an abundant cellular stroma, and might almost be described as consisting of granulation-tissue. The epidermal strata are occasionally absent, but they may be present and notably hypertrophied. Scales and crusts of epidermal cells are frequently formed.

395. **Acquired elephantiasis** (*elephantiasis arabum, pachydermia*) is a chronic and extensive hyperplasia of the skin and subcutaneous tissue. The various affections which have been described as elephantiasis (arabum) are certainly not all of the same nature; but if we except what is sometimes called elephantiasis mollis or fibroma molluscum (Art. 399), an affection depending on some congenital condition, they are all associated with some cause which gives rise to long-continued or often-repeated inflammation of the integument.

We said in Art. 394 that eczema was sometimes to be regarded as an inflammatory process leading to hypertrophy of the papillæ. This hypertrophy may extend to the cutis and subcutaneous tissues and lead to notable thickening of the entire skin, especially in the legs. Other chronic inflammations may like eczema lead to a pachydermatous condition of the skin: such are, for instance, chronic varicose ulcers, and chronic inflammation of bones lying immediately underneath the skin. Many of the forms of elephantiasis, and especially those to which the name is more properly restricted, take their rise in frequently-recurring erysipelatous inflammation. Tropical elephantiasis is now generally recognized to be ultimately due to the presence of the *Filaria sanguinis hominis* (Art. 235), a parasite which infests the lymphatics of the scrotum and lower limbs, and gives rise to inflammation and obstruction of the lymph-current.

Acquired elephantiasis may affect very various parts of the body, but is chiefly met with in the genitals and lower limbs. The enormous thickening and overgrowth of the integuments lead to great deformity, which is especially noticeable in the case of the lower limbs. As the leg becomes more and more thickened the distinction between foot and leg is gradually lost, and the limb at length looks like an elephant's. The scrotum may grow till it forms an enormous tumor reaching to the knees or lower, and may weigh upwards of a hundred pounds.

396. The affected parts of the skin in elephantiasis may be dense, hard, rough, and white (*elephantiasis dura*), or soft and grayish (*elephantiasis mollis*). When the tissue is cut into, a more or less abundant escape of lymph takes place: where the lymphatics are much dilated (*elephantiasis lymphangiectatica*) the lymph may flow away in considerable quantity.

The blood-vessels may be dilated and hypertrophied, or altogether unaltered. The subcutaneous and even the deeper-lying connective tissue may be involved in the general hypertrophy. The surface is either smooth (*elephantiasis glabra*), the horny layer being unaffected, or rough and warty (*elephantiasis verrucosa*), or tuberculated (*elephantiasis tube-*

rosa], or covered with papillomatous excrescences (*elephantiasis papillomatosa*). The horny layer is frequently thickened and altered, forming a covering of coherent scales or plates: the condition is sometimes described as acquired ichthyosis (Art. 397) or keratosis.

The structure of these elephantoid thickenings varies greatly. When they follow upon eczematous or ulcerative affections they are usually cellular and akin to granulation-tissue: sometimes they contain nodular aggregations of cells exactly resembling tubercles, and the lymphatics and the tissue around them are crammed full of lymphoid cells. On the other hand the tissue is in many cases poor in cells and coarsely fibrous in texture, giving one the impression that the normal fibrillæ are not so much increased in number as in individual thickness. Between these extremes there are numerous transitional forms, varying in the proportion of cells they contain and in the coarseness and abundance of the fibre.

The hyperplasia is in general uniform, but cases occur in which the thickened tissue is beset with irregular nodules, or in which the new tissue is more abundant round the sweat-glands and hair follicles. The papillæ are more or less enlarged.

The hyperplasia is probably to be regarded as resulting from an over-nutrition of the parts, which again depends on some inflammatory alteration of the vessels. Cell-multiplication is further favored by the partial occlusion of the lymphatics. This obstruction is well marked within the lymphatic glands, which are often hyperplastic in consequence of chronic inflammation. The production of lymph being increased and its outflow impeded, the tissues become saturated and the lymphatic vessels notably enlarged.

Scleroderma is a rare and very peculiar affection of unknown origin, which attacks adults. It takes the form of local or general stiffening and hardening of the skin without any apparent external cause: it is somewhat rapid in its onset, and then remains stationary or passes away, to be succeeded by a fresh attack or by a condition of cutaneous atrophy. It affects the face, limbs, and trunk; the patient often being literally 'hide-bound.' The skin feels as hard as a board, or like that of a frozen corpse (Kaposi). It is said that the fibrous tissues of the skin are hyperplastic and here and there infiltrated with small cells (Chiari, *Viertelj. f. Derm. u. Syph.* v.; for cases see Duhring, *Diseases of the skin* 1882). In one case of the disease Heller (*Arch. f. klin. Med.* x.) found that the thoracic duct was obliterated.

Sclerema neonatorum is a hardening of the subcutaneous connective tissue met with in infants, and chiefly affecting the legs and feet. According to Langer (*Wiener Sitzungsber.* 1881), it is due to the solidification of the *panniculus adiposus* by cold when the infant becomes collapsed. The fat of children contain more palmitin and stearin and less olein than that of adults: it solidifies at 45° C. Adult fat at ordinary temperatures separates into two layers: the upper or liquid layer solidifies at 0° C., the lower or semi-solid layer liquefies at 36° C.

CHAPTER XL.

NON-INFLAMMATORY HYPERTROPHIES AND TUMORS.

397. **Ichthyosis** is a general affection or deformity of the skin, characterized by the formation of epidermal scales and plates, and of warty growths. It consists in an excessive proliferation of the cutis and epidermis; and is hereditary and congenital, though it does not usually manifest itself till the first or second year of life. LELOIR has in two cases found the cutaneous nerves in a degenerate condition, and regards the disease as of nervous origin.

The horny layer is enormously thickened, laminated, and fissured (Fig. 156 *a*); the rete Malpighii on the other hand is slightly developed in comparison, and passes without transition into the horny layer. In *ichthyosis simplex* the papillæ are not enlarged. In very slight cases the skin is simply beset with small nodules (KAPOSI) covered with a thin scale and containing a coiled-up hair (*lichen pilaris*). This condition is met with chiefly on the exterior surfaces of the limbs. In more marked cases contiguous scales or plates of various sizes up to that of a sixpence are formed, giving the surface the look of crocodile-skin (*ichthyosis nitida*). These may subsequently become rough and dirty or discolored (*ichthyosis nigricans*). When the papillæ are hypertrophied as well as the epidermis, the surface becomes extraordinarily rough and irregular: sometimes the elevations stand up like quills upon a hedgehog (*ichthyosis hystrix*, Fig. 156.

EULENBURG, AMOZAN, and GEBER state that ichthyosis may occur as an acquired affection in the adult, in consequence of neuritis or injury to cutaneous nerves.

The peculiar affection which has been called **neuropathic papilloma** of the skin by GERHARDT, and neuropathic nævus by SIMON, seems to be closely akin to if not identical with ichthyosis. It consists of papillary elevations of the skin covered with fissured and loosened epidermis: the elevations may be pigmented. It is accompanied by certain neurotic symptoms; it often corresponds in distribution with the course of particular cutaneous nerves, and when unilateral ceases at the middle line of the body. For these reasons it has been regarded as of nervous origin (BEIGEL, GERHARDT, HARDY, VON RECKLINGHAUSEN). So far as we know it is congenital, or developed only in the first years of life.

True ichthyosis must be distinguished from the pseudo-ichthyotic condition which is a common result of cutaneous inflammation, and from the affection known as *ichthyosis sebacea* (Art. 403).

References on ichthyosis:—HEBRA, *Diseases of the skin* III.; NEUMANN, *Lehrb. d. Hautkr.*; ESOFF, *Virch. Arch.* vol. 69; LELOIR, *Arch. d physiol.* 1881; KYBER, *Wiener med. Jahrb.* 1880 (the case of an infant is described who was born with universal rigid mail-like thickening of the horny layer, an instance of so-called diffuse keratoma).

References on neuropathic papilloma:—BEIGEL, *Virch. Arch.* vol. 47; GERHARDT, *Jahrb. f. Kinderheilk.* 1871; VON RECKLINGHAUSEN, *Die multiplen Fibrome d. Haut* Berlin 1882 (the papillomata are thought to be due to congenital neuritis, the proximate cause being disturbance of the vaso-motor mechanism).

FIG. 156. ICHTHYOSIS HYSTRIX.
(*After KAPOSI: low magnification.*)

a, horny layer. *b*, rete Malpighii.
c, enlarged papillæ, infiltrated with cells and containing dilated blood-vessels *d*.
e, corium with coarse fibrous bundles and numerous vessels.

BOSTRÖM some time ago (*Situngsber. d. phys.-med. Gesell. zu Erlangen* 1880) described a case in which every three or four months the horny epidermis of the hand was shed in the form of a glove. This was preceded by intense redness of the skin, and coincided in time with a menstrual period. The affection was therefore not improbably due to vaso-motor disturbance.

398. **Warts and moles.** The skin is the seat of certain peculiar formations, which are characterized by the presence of nests and clusters of

epithelioid cells. They affect the cutis chiefly, and appear at birth or in the first ten or twenty years of life.

The nests and clusters (Fig 157 *d*) consist of epithelioid cells with large oval vesicular nuclei. They lie in the lower reticular layers of the cutis or in the papillæ, and are separated by vascular connective tissue: but there are neither vessels nor fibrous tissue in the cell-clusters themselves. When the clusters are few in number they give rise to no visible change on the surface of the skin, but when they are more abundant they cause the surface layers to project into small flattened or tuberous prominences.

The groups of cells are in general distinct from each other, and occa-

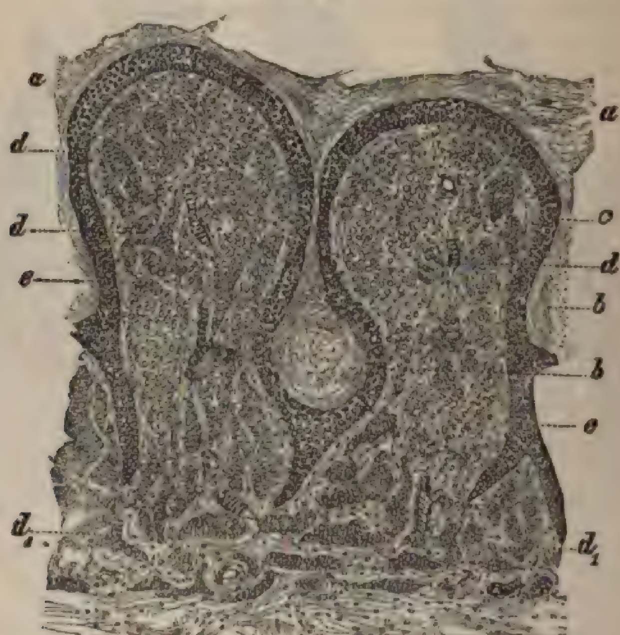


FIG. 157. SECTION THROUGH TWO PAPILLÆ FROM A CUTANEOUS WART.

(*Carmine staining:* × 50.)

a, thickened horny layer of the epidermis.
b, 'pearl' of epidermal cells.
c, rete Malpighii.
d, cell-nests and clusters in the papillæ, and
d_1, in the reticular tissue of the cutis.
e, vascular connective tissue.

sionally exhibit a certain regularity of arrangement into columns disposed at right angles to the surface of the skin. When they are very abundant and the intervening fibrous tissue scanty, the regularity is lost and the affected part seems made up of cells scattered uniformly through the tissue and separated partly by blood-vessels.

The overlying epidermis and the interposed fibrous tissue frequently contain yellow or brown pigment, but the cells themselves rarely contain

any. Such pigmented spots form the basis of freckles, sun-spots, mother's marks, warts, moles, and pigmentary nævi.

Freckles (*ephelides*) are small irregular brownish spots seen, usually on the face, in young people, and generally disappearing with advancing years. They sometimes however persist throughout life. Mother's marks (*lentigines*) are larger and more definite in size and dark-brown in color; they are either congenital or appear in infancy, and then remain unchanged throughout life. Moles and pigmentary nævi are congenital patches of various sizes, either level with the skin or slightly raised, and varying from yellow to brownish-black in color. They are often beset with hairs which are stronger and stouter than those in the neighboring skin; they are then called hairy moles (*nævi pilosi*).

Warts (verrucæ) vary in diameter from 1 to 20 millimetres. When the characteristic clusters of cells lie chiefly in the cutis and only to a small extent in the papillæ, the surface of the wart is smooth. When the papillæ are more extensively invaded (Fig. 158 *e*) the surface becomes somewhat rough and tuberous. When they constitute the chief seat of

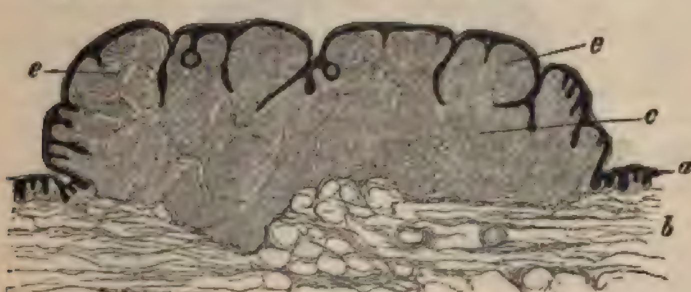


FIG. 158. SECTION THROUGH A SOFT WART.
(*Aniline-brown staining:* × 10.)

a, epidermis
b, cutis.
c, cellular growth in the cutis.
e, cellular growth in the papillæ.

the cellular growth, they become enlarged and elongated, and the wart becomes papillomatous.

The epidermis covering a smooth wart is not usually thickened, and the wart is therefore soft (*verruca mollis* or *carnea*). In the case of rough warts the epidermis is generally hypertrophied (Fig. 157 *a*), and between the elongated papillæ are formed dense concentric clusters or 'pearls' of horny cells (Fig. 157 *b*); the wart is therefore hard (*verruca dura*).

The significance of these cutaneous growths in relation to the ætiology of tumors has already been discussed (Art. 179). Inasmuch as they are usually congenital or appear in the first few years of life, it is not unnatural to regard them as untransformed remnants of embryonal tissue, which on occasion proceed to grow and to develop after birth. DEMIÉVILLE has recently (*Virch. Arch.* vol. 81) investigated the nature of pigmentary moles and nævi, and thinks the cellular

nests and clusters are derived from the adventitia of the blood-vessels. VON RECKLINGHAUSEN (*Die multiplen Fibrome der Haut* Berlin 1882), who deals mainly with soft warts, thinks the cell-groups are developed in the lymphatics and lymph-spaces, and regards the growth as a lymphangio-fibroma. The name cannot be regarded as very apt, for the term fibroma is inapplicable to a structure almost wholly made up of cells. VON RECKLINGHAUSEN makes out that the cells first appear in the papillary layer of the cutis, and penetrate from this into the substance of the papillæ themselves; but this is true only in certain cases. In papillomatous warts and in the smaller pigmented moles the characteristic cells often lie altogether or nearly so in the papillæ. When the cell-groups are few in number they are seen to lie around the vessels, but when they are more numerous no such relation can be made out.

399. **Fibromata** of the skin are of two kinds, the hard and the soft. The soft variety is the more common, and is referred to as **fibroma molluscum.**

The tumors so called vary in size from that of a millet-seed to that of a man's head. The smallest of them lie embedded and hidden in the

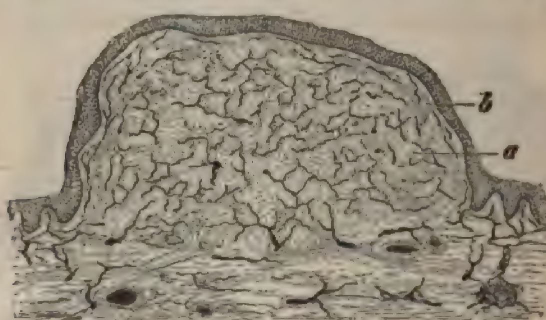


FIG. 159. FIBROMA (NEUROFIBROMA) MOLLUSCUM.

(*Injected preparation, stained with hæmatoxylin;* × 25.)

a, vascular fibrous tissue.

b, papilla thinned and flattened out by distention.

skin, but the larger ones (often spoken of as 'wens,' Art. 404) are generally protuberant and often stalked (*fibroma pendulum*). They are always soft and flaccid, and the surface is usually wrinkled. As a rule they are multiple and sometimes appear in enormous numbers, so that the skin is thickly beset with smooth or wrinkled or pendulous growths of all sizes. The skin of the trunk is the favorite seat. There are usually a few large tuberous growths among the multitude of smaller ones.

The tumors consist of grayish semi-translucent moist-looking tissue, composed of thin flattened spindle-cells and delicate fibrillæ.

Some forms are firmer than others; the less firm varieties are rich in small cells and the fibrillation of the intercellular tissue is indistinct; the firmer varieties have fewer cells and are markedly fibrous, but in no case is the tissue so coarsely fibrous as that of the normal cutis. The growths are developed in the reticular layer of the cutis (Fig. 159), and

when they project above the surface of the skin the papillæ are thinned and flattened out. The new-formed tissue may invade the papillæ directly, or may advance into the subcutaneous tissues.

Von Recklinghausen by his careful and exhaustive researches has established the fact that the multiple fibromata of the skin are in reality neurofibromata or neuromatous fibromata (Art. 154). They are developed from the fibrous sheaths of the smaller cutaneous nerves, and thence invade the fibrous structures of the vessels, the sweat-glands and their ducts, and the hair-follicles. The softer varieties still contain nerve-fibres, which run axially through the tumors, or subdivide and lose themselves in their substance. In the firmer tumors the nerve-fibres cannot be traced. The fibrous change (hyperplasia) extends some little way up the nerve-fibre from the point where it enters the tumor.

When a fibroma is carefully dissected it is seen to be made up of strands of dense fibrous tissue lying parallel to each other and united by loose cross-fibres. The structure of the whole growth is in fact plexiform, and so resembles that of the small neurofibromata which are found seated directly on the nerves.

Multiple cutaneous neurofibroma is either congenital or begins to appear in infancy: it is never truly an acquired affection. Many cases have been shown to be hereditary. Where a predisposition is known to exist, frequently recurring irritation sometimes leads to the development of the affection. Very frequently it is accompanied by the growth of fibromatous tumors on the deeper nerve-trunks, which accords with the view of its nature already expressed.

As the tumors grow they invade the fibrous sheaths of the various tubular structures seated in the skin, and occasionally reach an enormous size. In this case they give rise to the appearance of elephantiasis, the affection having on this ground being described as pachydermatocele (Valentine Mott), elephantoid molluscum (Nelaton), and elephantiasis mollis (Virchow); to distinguish it from acquired elephantiasis (Art. 395) we may perhaps designate it congenital elephantiasis. The affection does not always take the form of circumscribed tumors, but sometimes gives rise to extensive and general thickening and overgrowth of the skin (dermatolysis), which lies in loose overlapping bulges and folds like that of a hippopotamus or elephant.

Fibromata of various sizes are met with which are not neuromatous. They form hard or soft nodes seated in the skin or subcutaneous tissues.

Keloid is a very rare variety of fibroma. It takes the form of tuberous or discoid or band-like growths seated in the corium beneath the papillary layer. The papillæ and epidermis are intact. When fully developed the growth consists almost exclusively of bundles of coarse fibres. In its earlier stages it contains numerous spindle-cells.

Cicatricial keloid must be distinguished from true or spontaneous keloid. It grows in the substance of a scar, and is therefore not covered

with papillæ. In other respects it may resemble the true keloid. The disease called 'Addison's keloid,' and now known as morphœa, is in no way related to these affections: it is a hypertrophic condition, somewhat resembling scleroderma (Art. 396).

The genesis and significance of the multiple cutaneous fibromata have been worked out by VON RECKLINGHAUSEN (*Die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen* Berlin 1882). He investigated with the utmost care their relations to the various constituents of the skin and their developments from the fibrous sheaths of the nerves, and thus made clear many facts that were before unexplained. He also examined their connection with the fibromata (false neuromata) of the nerve-trunks, and with several allied affections of the skin such as elephantiasis mollis. BRUNS (*Virch. Arch.* vol. 50) and CZERNY (*Langenbeck's Arch.* XVII.) had already pointed out the close connection of the latter affection with multiple neurofibroma. VON RECKLINGHAUSEN gives in his tract a summary of the hitherto published cases and memoirs. He regards the elephantoid hypertrophic folds of the skin, referred to in the text as dermatolysis, not as due to the extension of a neurofibromatous growth, but as a primary neuropathic affection similar to neuropathic papilloma.

LABBÉ and LEGROS (*Journ. de l'anat. et de la physiologie* 1881) describe a circumscribed hypertrophy of the papillæ associated with hyperplasia of the touch-corpuscles. They call it papillary neuroma.

On keloid see LANGHANS (*Virch. Arch.* vol. 40); BABESIU (*Viertelj. f. Derm. u. Syph.* VII.); WARREN (*Sitzungsber d. Wiener Akad.* 1868); FAGGE (*Guy's Hosp. Rep.* 1868); KAPOSI (*Hebra's Diseases of the skin* III., with further references); DUHRING (*Diseases of the skin* 1882).

400. In addition to the inflammatory and tumor-like cutaneous growths there are others (mostly in the form of warty thickenings of the skin) in which all the constituent elements of the skin take part without any notable change of structure. They are most frequently met with in the face and form gland-like often hairy prominences. On the nose they appear as large irregularly lobulated swellings known as **rhinophymata** (HEBRA). They consist essentially of a thickening of the fibrous tissue of the skin with hyperplasia and cystic dilatation of the sebaceous glands: occasionally adipose tissue is developed in the thickened cutis. The result is the elevation of the papillary layer with the overlying epidermis (thickened or not) into circumscribed projections.

Molluscum contagiosum (*epithelioma molluscum, molluscum epitheliale,* sebaceous wart, endocystic condyloma) is the term commonly used to designate a peculiar tumor-like growth in the skin, the variety of other names proposed indicating that authors are not yet agreed on the exact pathological significance of the affection.

Some English and French authors, with HEBRA and KAPOSI, regard *molluscum contagiosum* as due to a distention of the sebaceous glands with accumulated cells, in which some of the cells undergo a peculiar metamorphosis. Others like VIRCHOW, BIZZOZERO, MANFREDI, PERLS, and THIN, consider it to be a purely epidermal growth not starting in the sebaceous glands. According to them it is a simple hyperplastic

growth of epidermal cells, starting in the hair-follicles (VIRCHOW) or in the interpapillary portion of the rete Malpighii (BIZZOZERO, MANFREDI). Nodes as large as a pea or larger are thus formed, and may be grouped in clusters. On section their structure appears to be racemose or gland-like, the nodes being made up of nests of epidermal cells separated by fibrous septa. The cells on the outside of the clusters are columnar. In the centre of the nests lie peculiar bodies like swollen starch-grains, either free or enclosed in cells. These bodies are characteristic of the affection, and are by some regarded as degenerate epithelial or epidermal cells, by others (KLEBS, BOLLINGER) as parasitic organisms. As the affection occasionally appears simultaneously in persons who live together it is often regarded as contagious (VIRCHOW); but this is denied by other observers, and apparently with good reason.

The name *molluscum contagiosum* is due to BATEMAN (*Delineations of cutaneous diseases* (Plate LXI.) London 1817). VIRCHOW regards the contagiousness of the disease as established *Virch. Arch.* vol. 33, and names it *epithelioma*. O. SIMON (*Deutsch. med. Woch.* 1876), C. BÖCK (*Viertelj. f. Derm. u. Syph.* II.), BIZZOZERO and MANFREDI (*Arch. p. l. scienze med.* I.) hold that the disease originates in a redundant multiplication of the cells of the rete Malpighii. The latter authors also describe how the characteristic 'molluscum bodies' are derived from epidermal cells. According to THIN (*Journ. of Anat. and Physiol.* 1881) groups of small granules make their appearance in the cells of the hair-follicles, and then in those of the surface layers of the skin; these granules are afterwards transformed into homogeneous masses. The epidermal cells begin then to grow downwards into the fibrous layers of the cutis, and in the growing cells similar homogeneous bodies appear.

For cases see FAGGE (*Guy's Hosp. Rep.* 1870), DYCE DUCKWORTH (*St. Barth. Hosp. Rep.* 1868, 1870), HUTCHINSON (*Clinical Surgery* vol. I. London 1878), MORISON, THIN, etc. (*Path. Soc. Trans.* 1881).

As against the contagious nature of the affection it may be mentioned that inoculation with the matter taken from the tumors does not tend to reproduce it.

401. Among the connective-tissue growths starting in the cutis angioma, lymphangioma, and sarcoma are somewhat common forms.

Angiomata appear as bright or dark red often slightly-raised patches in the skin. They have already been discussed in Arts. 148–151; and the lymphangiomata, which when extensive give rise to soft tuberous swellings without discoloration, have been referred to in Art. 152.

Sarcoma takes the form of nodular tumors, more or less raised above the surrounding surface; sometimes they are even pedunculated or mushroom-shaped. They are usually solitary, but now and then instances occur in which a number of sarcomatous growths appear in the skin simultaneously or in quick succession. Cutaneous sarcoma may be round-celled, spindle-celled, or mixed. The commonest form is the **round-celled,** of which both large-celled (Fig. 50, Art. 159) and small-celled varieties occur. Melanotic and alveolar sarcomata are also not uncommon. The latter (Fig. 54, Art. 161) start in cellular warts and pigment-spots, and correspond closely with these in their general struc-

ture. When they start in pigment-spots or pigmentary moles the substance of the tumor is pigmented. Like other round-celled sarcomata these are malignant. Spindle-celled forms may also start in warts or cutaneous fibromata. But all the forms may arise in portions of skin that previously appear altogether normal.

Lipomata of the skin and subcutaneous tissue are very frequently met with, and sometimes reach a great size. The region of the shoulder is a favorite seat.

Myxoma and enchondroma are less common than lipoma, and osteoma is rarer still. Myxoma and myxofibroma are generally connected with the external genitals in women.

Xanthelasma or xanthoma is a peculiar growth, taking the form of pale or brownish yellow circumscribed patches (*xanthelasma planum*) or nodules (*xanthelasma tuberosum*), which may be isolated or aggregated into groups. It occurs chiefly in the neighborhood of the eyelids and on the cheeks, and consists of a hyperplasia or new-formation of fibrous tissue, in which fat is subsequently deposited. Similar spots and nodules, often described as xanthoma, are produced on the eyelids by the enlargement of the meibomian glands and the deposit in the overlying skin of a pale yellow pigment. Occasionally the affection becomes multiple, or even universal (*xanthelasma multiplex*). In many cases of this kind jaundice has preceded the skin affection, and some authors have regarded the latter as connected with the circulation of bile-pigment in the blood. This is certainly not true of all cases.

402. **Epithelioma** (cutaneous cancer or cancroid) is by far the most important of the epithelial neoplasms of the skin. Its mode of growth has already been described in Art. 170 (see Fig. 62). The epithelial proliferation may start not only in the epidermis, but in the epithelium of the sebaceous glands of the hair-follicles. Three varieties might thus be distinguished, but a more useful distinction is that based on the general characters and appearance of the growth, inasmuch as it is difficult or impossible to say in all cases whence it first started. THIERSCH distinguishes a flat or superficial and a deep or infiltrating form. The former is met with chiefly in the lip, forehead, and nose; and is characterized by the fact that the epithelial ingrowths and processes are short and shallow. It generally appears as a slightly raised ulcer with hardened or infiltrated borders, due to the breaking-down of a primary cancerous node. Its growth is usually very slow, and it may cicatrize at the centre while the marginal ulceration continues to advance. In other cases the process of disintegration is more rapid, and the ulcer steadily increases in depth and extent. This form is clinically described as **rodent ulcer,** and chiefly affects the upper part of the face. The stroma of an ulcerating cancer is always more or less infiltrated with cells, and these may be so abundant in some places as to give it the look of granulation-

tissue. The superficial form seldom produces metastatic growths in the lymphatic glands or elsewhere.

The deep or infiltrating form gives rise to irregularly-shaped ulcerations, due as in the former case to the breaking-down of nodular epithelial growths. From the floor and edges of the ulcer often rise large protuberant warty structures, giving the affection the appearance of a papillomatous tumor. This form produces metastases oftener than the other.

Intermediate forms are not uncommon which it would be difficult to class definitely with one or other of the above; and other varieties having no resemblance to either of them also occur. In fact the processes of cancerous infiltration, proliferation of the fibrous tissue, disintegration, and ulceration, may be combined in numerous ways, and give rise to great diversity of appearance in the several stages of the disease.

Epithelioma most frequently attacks parts where epidermis passes into mucous membrane—such as the lower lip, nose, eyelids, prepuce, anus, external female genitals, etc. Occasionally it seems to start in warts or callosities or in scars.

Some English pathologists insist on the distinctions between ordinary epithelioma and what is clinically called rodent ulcer by English surgeons. One distinction drawn is that in the former the neoplastic cells are recognizably of an epidermal type, in rodent ulcer they are epithelial but not epidermal, having small nuclei and but little stability, as if derived from glandular cells: they have been supposed to be derived from the cells of the sweat-glands (THIN) or of the outer-root sheath of the hairs (FOX). See THIERSCH (*Der Epithelialkrebs* Leipzig 1865), MOORE (*Rodent Cancer* London 1867), WARREN (*Rodent Ulcer* Boston, 1872, *Med. Times and Gaz.* 1, 1880), HUTCHINSON (*Clinical Surgery* vol. I. London, 1875), THIN, FOX, BUTLIN, and others (*Path. Soc. Trans.* 1878–79, in which references to earlier literature will be found), KAPOSI (*Hebra's Diseases of the skin* IV., *Path. u. Therap. d. Hautkrankheiten* Vienna 1880).

Adenoma of the sweat-glands is a somewhat rare affection. It gives rise to nodules, which break down and ulcerate (VERNEUIL, *Arch. générales* 1854; THIERSCH, *Der Epithelialkrebs* 1865).

Secondary neoplasms of the skin are not very common, though they do occur in connection with both connective-tissue and epithelial tumors. Malignant growths of the skin itself are especially apt to infect healthy parts of it, and give rise to daughter-tumors. Of growths in other organs mammary cancer is the most apt to produce cutaneous metastases.

CHAPTER XLI.

AFFECTIONS OF THE SEBACEOUS GLANDS, HAIR, AND NAILS.

403. **Disorders of the sebaceous secretion.** In normal conditions the epithelium of the sebaceous glands secretes a small quantity of oily liquid, which becomes condensed in the gland or in its duct to a semi-fluid grease-like substance containing disintegrated cells. If the secretion becomes over-abundant we have what is called **seborrhœa** or steatorrhœa, with its consequences which go by the various names of *tinea furfuracea, acne sebacea, ichthyosis sebacea,* etc. According as the secretion dries into scales and crusts or remains liquid and oily we have *seborrhœa sicca, squamosa, furfuracea,* or *seborrhœa oleosa.*

The scales and crusts are often dirty and discolored, and occasionally form broad greasy scabs or lamellæ, from the under side of which processes pass into the openings of the sebaceous ducts.

Seborrhœa may be local or general. The local variety chiefly affects the scalp and the external genitals. General seborrhœa is rare, and is usually met with only in new-born infants; the abundant secretion of *vernix caseosa* which is normal in the intra-uterine period is in fact continued after birth. The abundant sebaceous secretion from the glands of the scalp which is normal during the first year of life sometimes gives rise, in neglected infants, to large fissured dirty cheesy-looking crusts or cakes, consisting of fatty matter, dirt, epidermal scales, and hairs.

Seborrhœa often affects enfeebled or anæmic patients. The skin of the trunk and limbs becomes covered with dry glistening scales, whence the affection is sometimes referred to as *pityriasis tabescentium.* When the scalp only is affected, the dried secretion taking the form of abundant branny scales, the affection is called **dandriff** or *pityriasis furfuracea capillitii;* when the scales are large and thick it is sometimes called *ichthyosis sebacea.*

Asteatosis, in which the sebaceous secretion is diminished, is rare as an idiopathic affection. It is usually secondary to other affections like ichthyosis, prurigo, psoriasis, pityriasis rubra, leprosy, etc. The skin becomes dry and fissured, and is shed in scales or flakes.

404. Various disorders of the skin are due to the accumulation of sebum in the glands or ducts in consequence of some obstruction of the outlet. The obstruction is usually due to the drying of sebum or the deposit of dirt at the mouth of the duct.

Comedones are small elevations of the skin due to plugging of the sebaceous ducts, or of the common opening of duct and hair-follicle. When the plug is squeezed out it appears as a whitish and somewhat firm pear-shaped or cylindrical mass of the size of a pin-head, the superficial end being stained black or brown. It consists of sebum and horny epidermal cells, and often contains minute hairs, and the mite called *Demodex folliculorum* (Art. 225). According to UNNA (*Virch. Arch.* vol. 82), the staining of the 'head' of the comedo is due to the presence of pigment either free or contained in the horny epidermal cells. Comedones usually occur on the forehead, cheeks, and chin, and occasionally the chest.

Milium (*grutum* or *acne albida*) consists of small roundish white or yellowish elevations of the skin, due to the accumulation of sebum and epidermal cells in sebaceous glands whose outlet has become obliterated. Occasionally the accumulation may distend the tubes of the associated hair-follicles into cysts of considerable size. The skin of the eyelids is a favorite seat. When the nodule is incised and the contents evacuated, they are often found to be concreted into a firm and sometimes even stony core.

Wens or sebaceous cysts (*atheroma* or *steatoma*) are due to the collection of more or less fluid secretion distending the lumen of the sebaceous gland, its duct, and the neighboring hair-follicle into a cyst, which may be as large as a walnut or even considerably larger. The contents of a wen may be soft and pulpy or firm and friable. They consist of fatty detritus, sebum, epidermal cells, and sometimes tablets of cholesterin and hairs, all enclosed in a capsule made up of layers of epithelial cells and fibrous tissue. They are usually seated on the scalp, more rarely on the back of the neck or on the face, trunk, and limbs.

Sometimes papillary outgrowths covered with epidermoid cells arise from the inner surface of the wall of a sebaceous cyst, and may increase in size so as to fill up the cavity. FÖRSTER (*Würzburger Verhandlungen* x.) has described this as dry cancroid: it may in time become calcified. CHIARI (*Naturforscherversamm. in Salzburg* 1881) has met with a case in which the internal layers of cells became dry and horny, the fibrous capsule becoming at the same time contracted. Atheromatous cysts are sometimes formed at the site of persistent branchial clefts (Art. 8).

405. **Inflammatory affections of the sebaceous glands and hair-follicles.** **Acne** is the general name given to localized inflammations surrounding the hair-follicles and associated sebaceous glands (Fig. 160). It gives rise to small red nodules or pimples, in which may be noticed the dark head of a comedo, or a minute collection of pus.

The tissue around the hair-follicle and gland may be simply hyperæmic and infiltrated with cells (Fig. 160 *b*), or suppurating; and according to the intensity of the inflammation are distinguished the varieties *acne indurata*, *acne punctata*, and *acne pustulosa*. The extent of the

inflammation also varies greatly. Ultimately however the sebaceous gland, and often the hair-follicle also, are destroyed.

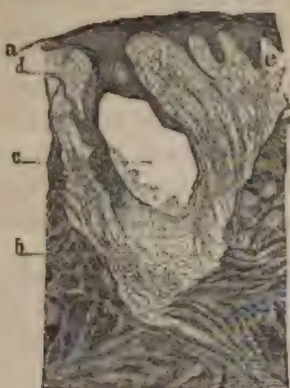


FIG. 160.

VERTICAL SECTION THROUGH AN ACNE-PUSTULE.

(*After KAPOSI: slightly magnified.*)

a, epidermis.

b, inflammatory infiltration of the corium surrounding the gland and hair-follicle and of the neighboring papillæ *e*.

c, sebaceous gland the contents of which have been mostly evacuated; the remainder consists of pus and fatty epithelial detritus.

d, the hair-follicle connected with the gland (in oblique section).

e, altered papillæ.

The cause of the inflammation is probably to be found in some anomaly of the glandular secretion. It is easy to understand that if the secretion stagnates and becomes in some way contaminated, it may act as an irritant on the surrounding tissues.

Acne mentagra (*sycosis non-parasitaria* or *folliculitis barbæ*) is a suppurative peri-follicular inflammation. It gives rise to papules and pustules, which are usually perforated by hairs. The parts affected are the beard, and sometimes the scalp.

Parasitic sycosis resembles the non-parasitic affection; it is due to the invasion of a fungus (see under *tinea tonsurans*, Art. 411).

Boils or *furunculi* are due to inflammation of the tissue surrounding a hair-follicle or sebaceous gland, being distinguished from the pimples or pustules of acne by the much greater extent and intensity of the inflammation. A hard dark-red swelling is produced, containing in the centre a 'core' or slough of necrosed tissue: as the tissue around suppurates the core is loosened, and ultimately cast off when the boil 'breaks.'

Carbuncle or *anthrax simplex* resembles a boil in many points, being a firm more or less circumscribed deep-seated inflammation of the skin; but it extends over a greater area, and gives rise to a firm livid swelling which may reach the size of the palm of the hand or more. The swollen and infiltrated skin usually necroses, and is transformed into a dark grayish pulp or a continuous slough. The subcutaneous tissue becomes necrotic and suppurates beneath the slough, the pus usually breaking through at several points. The slough is ultimately cast off, leaving an open granulating wound.

406. **Lichen** (according to HEBRA and KAPOSI) is an eruption of papules, which remain as such throughout, and do not pass into any other form of efflorescence.

Lichen scrofulosus is a chronic affection, in which pink or brownish flattened papules are formed, each capped with a small scale. It is met with chiefly in scrofulous patients, and usually affects the trunk.

According to KAPOSI it is due to inflammatory infiltration and exudation in and around the hair-follicles and sebaceous glands, and in the neighboring papillæ. The scales are composed of epithelial cells which accumulate round the openings of the follicles.

Lichen ruber acuminatus is characterized by the appearance of scattered hard red nodules, each capped with a little knot of epidermal scales, and tending to coalesce into irregular desquamating patches. In the course of years the affection may extend over the entire surface of the body. The process starts in and around the hair-follicles (HEBRA, KAPOSI, NEUMANN), beginning with hyperplasia of the cells of the outer root-sheath; cellular outgrowths from the follicles penetrate the surrounding structures, and the papillæ and rete Malpighii become infiltrated with cells or themselves undergo proliferation. In *lichen ruber planus* the papules are flattened and umbilicated, they are red or dull pink, and the continuous patches into which they coalesce have a shining waxy look and do not desquamate.

407. **Affections of the hair and nails.** Each hair according to its size has a definite period of existence. When this is at an end, the hair is shed and its place is taken by a new one. The replacement is effected by the cells at the tip of the papilla ceasing to grow and multiply, in consequence of which the old hair with its inner root-sheath is separated from the papilla. The young hair is then produced by the renewed growth of the cells of the papilla left behind on the separation of the old hair. Long thick hairs live longer than short and fine ones.

To maintain the uniform growth of the hair as a whole a constant relation must be kept up between the loss of old hairs and the production of new. When this relation is disturbed by hindrances to production, the result is **alopecia** or baldness. KAPOSI distinguishes the following forms.

Alopecia adnata, or congenital absence of hair, is seldom an enduring condition.

Alopecia (*calvities*) *acquisita* is natural in old age (*alopecia senilis*), but it may appear at any period of life (*alopecia prematura*). In the baldness of age the skin exhibits the changes described in Art. 364; but it is to be noted that they do not appear till after the hair has disappeared; they cannot therefore be the cause of the baldness.

Alopecia prematura may be idiopathic or symptomatic. In the former case the hair falls off without visible disease of the skin. When the denudation takes the form of isolated patches the affection is described as *alopecia areata* (*area Celsi* or *porrigo decalvans*). In some instances it extends to every spot on which hair occurs. As to its cause, some authors regard it as a micro-parasitic affection (EICHHORST, *Virch. Arch.* vol. 78; LASSAR, *Deutsch. Med. Woch.* 1881; THIN, *Prog. Roy. Soc.* 1881, *Brit. Med. Journ.* 2, 1882, the associated fungus being named by him *Bacterium decalvans*), while others with much less reason speak of

it as a trophoneurosis. In senile alopecia obliteration of the capillaries supplying the hair papillæ has been noticed. In the premature form the follicles sometimes appear stunted and atrophied.

The causes of symptomatic alopecia are better understood. Any inflammatory process which seriously disorders the nutrition of the skin, such as eczema, erysipelas, acne, lupus, syphilitic eruptions, etc., may give rise to baldness. The continuous development of the hair from its bulb is interfered with, and the hair thus ceases to grow and is shed. If the papillæ are not destroyed the hair may afterwards be reproduced.

Alopecia due to chronic exudative affections of the skin, such as psoriasis, lichen ruber, or eczema, is described as *alopecia furfuracea* or *pityrodes*. Seborrhœa is a common cause of baldness. The hairs are imperfectly formed, and they therefore fall off sooner than they should do, they are replaced only by thin downy hairs, and after a time no new hair is produced at all.

The **nails** are frequently misformed or defective, and abnormally thin or brittle, especially as a result of inflammations or of direct injury.

408. **Overgrowth of hair** (*hypertrichosis, hirsuties, polytrichia*) may be congenital or acquired. The whole body or isolated parts of it may be abnormally hairy. Congenital hairiness seems to be hereditary in some families. Cases are known in which not only the trunk and limbs, but also the greater part of the face and even the nose, have been covered with hair. Hair on the chin and upper lip in women is not uncommon. Moles and pigment spots are often abnormally beset with hair (Art. 398).

Overgrowth of the nails in length and thickness is frequently met with, and they are often at the same time distorted, rough, or tuberculated. Excessively long nails become curved into claws (*onychogryphosis*). When they become excessively broad they are apt to cut into the soft parts, giving rise to hæmorrhage and inflammation (*paronychia*). Vegetable parasites sometimes attack the nail and its bed, which they penetrate in all directions, causing it to increase in size and ultimately to soften and break down (*onychomycosis*, Art. 411).

On hairy men (*homines pilosi* or *hirsuti*) see WILSON (*Diseases of the skin* London 1867, *Lectures on Dermatology* London 1878) and ECKER (*Ueb. abnorme Behaarung des Menschen* Brunswick 1878).

CHAPTER XLII.

PARASITIC AFFECTIONS.

409. **Vegetable parasites.** The hyphomycetes or moulds (Arts. 213, 222), which infest the human skin form jointed mycelial filaments (hyphæ) and spores (conidia) (Fig. 161). Various names are given to the groups of filaments and spores according to the form of the affection or **dermatomycosis** which they produce. The filaments and spores are found chiefly in the epidermoid structures of the skin, and especially in the hairs and hair-follicles. The filaments penetrate between the cells, loosen them from each other, and ultimately separate them from their nutrient base; the disintegrated cells then serve for a soil to the growing fungus. Hyperæmia and inflammation are set up, and in consequence scales, vesicles, pustules, and scabs, are developed. The fungi have no perceptible effect on the system as a whole. They do not attack all skins, but only those which exhibit a certain predisposition, though it is hard to say wherein this lies.

The mycoses of the skin are divisible into three main forms, known as Favus, Tinea tonsurans, and Pityriasis vesicolor.

In addition to these familiar dermatomycoses there are others which are also ascribed to the invasion of fungi, such as alopecia areata, psoriasis, and contagious impetigo. They have been already described. The bacterial affections of the skin have likewise been treated of; they are variola (Art. 388), erysipelas (Art. 375), phlegmon and malignant pustule (Art. 390), leprosy (Art. 133 and 392).

410. **Favus** (*tinea favosa* or crusted ringworm) chiefly attacks the scalp, though it is also met with in other parts, such as the nails. It is characterized by the formation of pale-yellow cup-shaped friable crusts usually perforated by hairs, the so-called favus-cups (*scutula*). The crusts vary from the size of a pin-head to that of a sixpence.

According to KAPOSI the favus-cup begins as a minute yellow punctiform spot perforated by a hair and lying beneath the epidermis. In a few weeks it grows to the size of a pin-head, and then appears as a pale-yellow cup-shaped disc showing through the skin. On section the disc (Fig. 162) is seen to consist of mycelial filaments and spores lying beneath the horny layer of the epidermis (absent in the figure) in an excavation of the skin. If the cup is removed the surface of the excavation has a red and moist appearance. The cup itself is whitish and friable, and

may be teased out when placed in water. The fungus is called *Achorion Schönleinii* (from SCHÖNLEIN who discovered it in 1839).

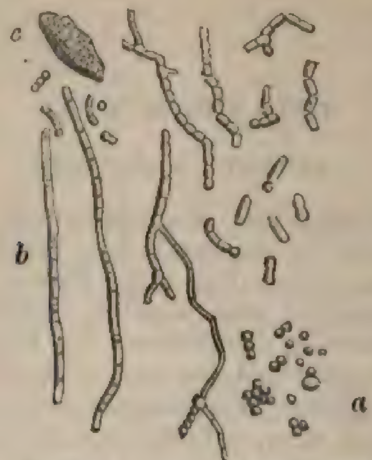


FIG. 161. FUNGI FROM A FRESH FAVUS-PATCH (*NEUMANN*).

a, separate conidia. *b*, mycelial filaments.
c, epidermal cell beset with micrococci.

FIG. 162. CUP OR SCUTULUM OF FAVUS (*NEUMANN*).

a, free edge of the cup.
b, dead and disintegrated horny layer of the epidermis.
c, *d*, mycelial filaments.
e, conidia.
f, epidermis.
g, altered papilla.
h, cellular infiltration beneath the cup.
i, cutis.

If the favus-cups are not removed they coalesce to form large con-

tinuous masses. When the horny skin which binds them down is cast off or broken through, these masses are exposed and dry up into yellowish mortar-like crusts. The hairs look dull and powdery and are easily pulled out. This is due to the fact that the hyphæ and conidia enter the opening of the hair-follicle and grow into the bulb and shaft of the hair (Fig. 163 *a*), and also into the root-sheaths.

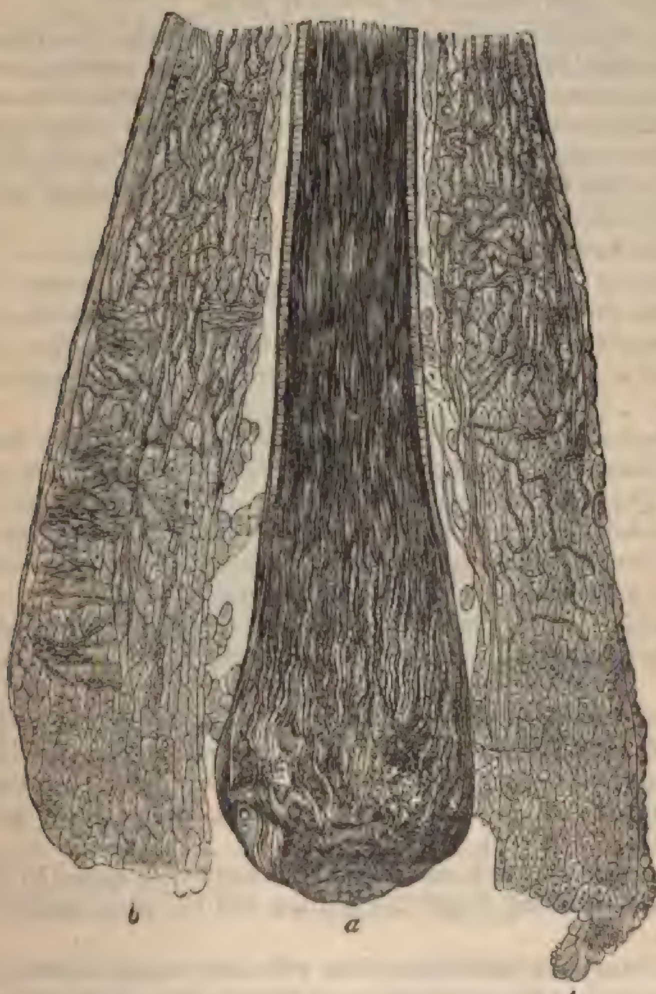


FIG. 163. HAIR AFFECTED WITH FAVUS (*after KAPOSI*).
a, hair-bulb and shaft.
b, root-sheath beset with hyphæ and conidiæ.

The hair may be actually extruded by the growing fungus, and the papillæ may become atrophied by pressure. At the same time the surrounding tissue is affected with more or less intense inflammation, which

may take on an eczematous character. When the fungus settles in the nail (*onychomycosis favosa*), yellowish deposits or thickenings are formed, and the substance of the nail becomes loosened and softened.

411. **Tinea tonsurans** (*herpes tonsurans* or common ringworm) is an affection produced by the filaments and spores of *Trichophyton tonsurans* (discovered by GRUBY in 1844). It assumes a different appearance according as it occurs on hairy or non-hairy parts.

Tinea tonsurans capillitii, or ringworm of the scalp, gives rise to bare circular patches from the size of a sixpence to that of a crown-piece, or to an irregularly scattered eruption, the hairs over the affected spots being broken off short and frayed at the ends. The surface of the patches is smoothed or scaly, and their margins are reddened. Vesicles and scabs are occasionally produced. The patches may be few or many, and grow steadily in size until the affection is cured.

On non-hairy parts rings of vesicles (*tinea* (*herpes*) *tonsurans vesiculosus*) and red scaly circular patches (*tinea tonsurans squamosus*) are produced, the affection being then generally described as *tinea circinata* or ringworm of the body. Sometimes a number of red spots appear in rapid succession at various points, and heal as rapidly without attaining any great size.

Trichophyton tonsurans forms long slender and but little branched mycelial filaments; it produces spores within the body, but the mycelium is not aggregated into scutula like that of *Achorion*. It readily penetrates the hair-shaft, making it brittle or rotten. In scaly ringworm of the body the fungus penetrates the upper layers of epidermal cells immediately underneath the horny layer (KAPOSI).

When the fungus attacks the nails (*onychomycosis tonsurans*), they become opaque and split into laminæ, becoming at the same time very brittle.

Sycosis parasitaria (*tinea sycosis* or barber's itch) is due to an inflammation of the skin and subcutaneous tissue accompanying the invasion by *Trichophyton* of the hairy parts of the face and neck. Exudation and suppuration are set up, and pustules, abscesses, and papillary growths, are the result (Art. 405).

Eczema marginatum is an eczematous inflammation caused by *Trichophyton*, and affecting chiefly the genitals and the parts around them (KAPOSI).

412. **Pityriasis versicolor** (*tinea versicolor, mycosis microsporina*) is characterized by the appearance of uniform pale or dark yellowish or brownish patches of various sizes and shapes, and either smooth and shining or dull and scaly on the surface. They occur chiefly on the trunk, neck, and flexor surfaces of the limbs, never on the hands or feet or on the face. The epidermis is readily scraped away from the patches, and is found to contain the filaments and spores of a fungus called *Microsporon furfur* (discovered by EICHSTEDT in 1846). It grows in the horny layer

of the epidermis and does not penetrate the hairs or their follicles. It does not usually set up any hyperæmia or inflammation.

Pityriasis rosea (GIBERT) or *pityriasis maculata* and *circinata* (BAZIN) is an affection of the skin resembling ringworm, and it is stated that it is due to a filamentous fungus. According to BEHREND (*Berl. klin. Woch.* 38 and 39, 1881; 34, 1882), who calls the disease *Roseola furfuracea herpetiformis*, it is characterized by the formation of prominent rosy spots from the size of a millet-seed to that of a bean, which are covered with powdery epidermal scales. They generally occur on the neck, and thence spread quickly over the body, leaving the head, hands, and feet unaffected. The spots disappear in two or three days. In some cases the epidermal scales contain spores and delicate mycelial filaments.

HEBRA recently described (*Wiener med. Blätter* 1881) a peculiar itching mycosis of the skin affecting the neck, elbows, and hams, and due to a fungus resembling that of pityriasis versicolor. Small shining grayish-yellow flattened papules are formed, which are grouped in clusters or arranged in long rows.

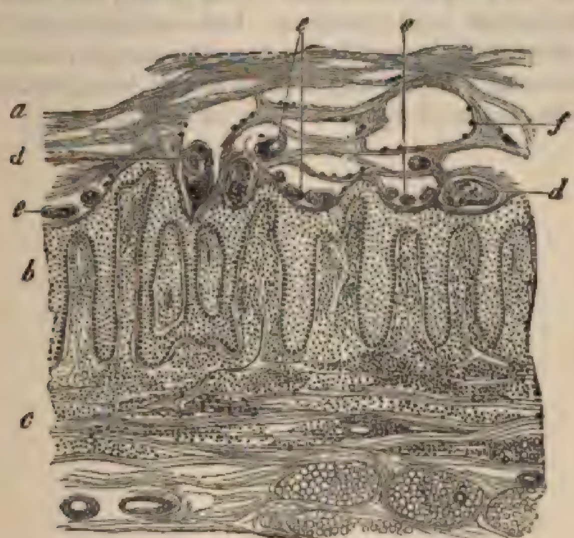


FIG. 164. SECTION OF THE SKIN IN SCABIES.

(*Carmine staining* : × 30.)

a, horny layer traversed by numerous burrows.
b, rete mucosum, with hypertrophied and infiltrated papillæ.
c, cutis infiltrated with cells.
d, section through an adult itch-mite.
e, eggs and embryos of various sizes.
f, excreta of the itch-mite.

413. **Animal parasites.** We have already described (in Arts. 225, 226, and 235) the various animals that infest the cutaneous tissues, and the affections to which they give rise. Here we need mention only **scabies** or itch, due to the settlement of the *Acarus scabiei* (Art. 225) in the epidermis.

The itch-mite pierces the horny layer and bores its way obliquely through it till it reaches the rete mucosum in the neighborhood of the papillæ. As the epidermal cells grow and approach the surface, it con-

tinues to work its way downwards so as always to keep below. In this way it gives rise to burrows (*cuniculi*) which penetrate the skin obliquely and are irregularly zigzagged and curved: they may reach the length of one or two centimetres. The mite sits at the blind end of the burrow (Fig. 164), leaving behind its excreta (*f*) in the form of yellow, brown, or black grains and lumps. The female also lays its eggs in the burrow, and as these are hatched the young mites may be seen in all stages of development (*e*).

The irritation caused by the mite directly and by the scratching which it induces gives rise to eczematous inflammation of the skin, with the formation of vesicles and pustules. Pus may collect beneath the burrows of the *Acarus*.

When the affection is allowed to become chronic the skin may be very gravely altered, the epidermal layers being greatly thickened and pervaded by the burrows in all directions. Inflammatory hypertrophy of the cutis takes place, and the papillæ (*b*) become enlarged and notably elongated. The horny layer (*a*) may become almost honeycombed or cavernous from the number of burrows which traverse it.

SECTION VI.

THE MUCOUS MEMBRANES.

CHAPTER XLIII.

STRUCTURE AND FUNCTIONS.

414. The **general structure** of a mucous membrane is similar to that of the skin, and its surface is everywhere in continuity with the exterior surface of the body. In textural details, however, there are considerable differences. The fibrous or reticular tissue (the **mucosa**) underlying the epithelial cells is looser and more cellular than the cutis; indeed in many parts it assumes the structure of **lymphadenoid tissue** and encloses a multitude of lymphoid elements in its meshes. The **epithelial covering** is thinner and more delicate than the epidermis, in some places consisting only of a single layer of juicy cylindrical cells; and even where the layers are numerous there is no protecting horny covering as in the case of the skin.

The mucous membranes are all well supplied with blood-vessels and lymphatics, which extend up to the epithelial strata. The vessels are in general continuous with those of the loose-textured and vascular submucous connective tissue (the **submucosa**). The submucosa is abundant in the mucous membranes of organs which are exposed to rapid and repeated changes of area and volume, and whose lining-membrane is consequently apt to be thrown into folds. In organs, like the uterus, which are not exposed to such sudden variations the submucosa is absent.

The epithelial covering of the mucous membranes is highly permeable; so that liquids and small corpuscular bodies pass in from the outer surface, or pass out and are excreted from the blood-vessels. These matters pass partly between the epithelial cells, and partly through their substance.

All the mucous membranes yield a secretion, which, apart from the liquid excreted from the vessels (usually small in amount), is characterized chiefly by the presence in it of **mucus.** The mucus is derived from certain of the epithelial cells, which elaborate it within their protoplasm and then extrude it. Lymphoid elements also escape from the reticular substructures, and passing between the epithelial cells reach the surface and form the swollen spherules known as **mucus-corpuscles.** According to Stöhr they are most abundant where the mucosa contains lymphadenoid tissue.

The mucus secreted by the membrane is of great service to it both in normal and in morbid conditions. It forms a protective covering,

and is often of use in warding off the effects of noxious substances or influences which may tend to affect the membrane injuriously. In certain circumstances the extruded lymphoid elements may act in a similar way. If the two together are insufficient to remove or to withstand the noxious agency, the mucous membrane undergoes more or less extensive alteration and injury.

Noxious matters also reach the membrane from within by way of the blood, but the injuries so produced are on the whole less important than the former class.

CHAPTER XLIV.

HYPERÆMIA AND HÆMORRHAGE.

415. **Congestive hyperæmia.** Many of the mucous membranes are physiologically subject to periodic hyperæmia. The blood-supply of the alimentary canal during digestion, and of the uterus during menstruation, is very strikingly increased. The increase is governed by vasomotor influences transmitted through the nerves, in obedience to which the afferent arteries are dilated, and so convey more blood to the parts.

Morbid influences may likewise give rise to hyperæmia, either by paralyzing the vaso-constrictor, or stimulating the vaso-dilator nerves. The morbid stimuli may act on the central nervous system, or, by reflex action, on the mucous membrane itself. The swallowing of hot food makes the stomach hyperæmic ; the inhalation of irritating vapors or the act of rubbing the eyelid will determine blood to the bronchi or the conjunctiva respectively.

A mucous membrane when hyperæmic becomes intensely reddened, and the distended vessels can be distinguished on close examination. At the same time the secretion becomes more abundant, often visibly so after the congestion has lasted a little time.

Passive hyperæmia or engorgement usually gives rise to livid redness; but if the membrane is exposed to the air (as in the case of the lungs) the tint may be almost arterial. Long-continued venous engorgement frequently leads to abiding varicose dilatation of the veins. If œdema results from the engorgement, the membrane usually swells up and assumes a sodden appearance. Where the submucosa is loose and open (as in the intestine) the swelling is sometimes very remarkable, the transuded liquid collecting in great abundance in the meshes of the tissue.

416. **Hæmorrhages** occur very frequently in the mucous membranes. They may be slight, giving rise merely to minute specks of ecchymosis and the mingling of a few red corpuscles with the ordinary secretion ; or so abundant that the membrane itself is soaked with blood, which at the same time pours away from the free surface. Excessive hæmorrhages of this kind often occur without any perceptible cause, especially in persons congenitally predisposed to bleeding (Art. 28). Many persons are particularly subject to bleeding from the nasal mucous membrane ; others bleed from the surface of the large or small intestine or from the bladder, sometimes to such an extent that death ensues. Congestion, thrombosis,

embolism, wounds, disease of the vessels, may any of them give rise to hæmorrhage, and some of the inflammations of the mucous membrane are apt to assume a hæmorrhagic character, or at least to be accompanied by extravasations of blood. Such extravasations may be due to diapedesis or to actual rupture of the vessels.

The consequences of hæmorrhage are various: small extravasations are re-absorbed, but often (as in the intestine) leave behind slaty or black discolorations which may persist for a long time. Frequently the tissue infiltrated with blood necroses and breaks down; erosions and ulcers are thus produced, which at times reach a considerable size. After extensive hæmorrhage, such as results from intense and enduring engorgement, large and continuous portions of the tissue may perish, and gangrene not uncommonly sets in.

CHAPTER XLV.

DEGENERATION, ATROPHY, AND HYPERTROPHY.

417. The various forms of retrogressive change described in Arts. 32–71 may all of them affect the mucous structures.

Necrosis occurs chiefly as the result of mechanical or chemical injury, and also of disorders of the circulation and inflammation. The changes produced are treated generally in Arts. 32–71, and with reference to particulars in Arts. 424–427. The issue of necrosis is always local inflammation and ulceration; repair takes place by regenerative growth, or by granulation and cicatrization.

In considering the various modes of degeneration it is convenient to separate the changes in the epithelial elements from those in the fibrous tissues of the mucous membrane. The former show signs of degenerative change much more frequently than the latter. One of the commonest manifestations is an abnormal increase of the mucous secretion (**catarrhal inflammation**, Art. 420). Fatty degeneration of the epithelial cells is also common; and abnormal and premature desquamation plays a considerable part in certain of the inflammatory processes. The fibrous structures are especially liable to **amyloid disease**, especially in the intestine. The walls of the vessels are the favorite seat of the degenerative change. The fibrous structures are sometimes affected by mucoid and fatty degeneration, but they are much less liable to such changes than the epithelium.

Atrophy of the mucous membrane, by which the epithelium is in part destroyed, is a condition of the greatest importance. In the alimentary canal the process can be followed in its most typical form; it is usually connected with or dependent on catarrhal inflammation.

It will be remembered that the mucosa of the intestine is mainly composed of a glandular stratum containing lieberkühnian crypts with the underlying muscularis mucosæ. The glandular stratum is about 0.4 to 0.5 mm. in thickness. In catarrhal conditions the epithelium is loosened and cast off in abnormal quantity; the fibrous tissue between the crypts is densely infiltrated, and often degenerates or suppurates (Art. 421, Fig. 167), so that the epithelium may in part be permanently lost. The glandular stratum is in consequence often wasted to the half or the third of its former thickness (Fig. 165), or the glands may disappear entirely (*e*) leaving nothing but a thin nucleated fibrous film.

The muscularis mucosæ is in general but slightly affected, though it too may become atrophied. The submucosa is usually little altered, unless the inflammation is very intense; and if the inflammation does not pass into ulceration, the lymphadenoid tissue of the mucosa remains almost intact.

The mucous membranes of the stomach, uterus, etc., are affected in much the same way. Their glands are usually atrophied or obliterated, but in some cases they may undergo a kind of cystic degeneration.

418. The **power of repair** which the mucous membranes possess is exemplified in the rapid restoration of lost epithelium. But this restoration is only complete if the underlying fibrous structures are themselves uninjured, or at least effectively restored. If from any cause a small portion of the fibrous coat is destroyed, the regeneration of the corresponding epithelium is imperfect. If the portion destroyed is of any

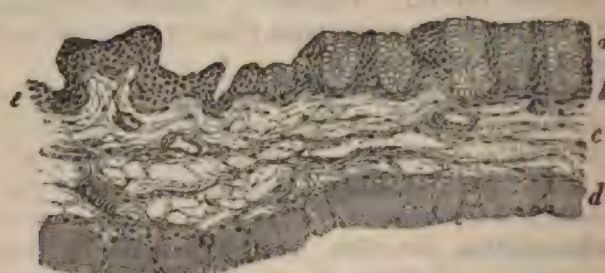


FIG. 165. MUCOSA AND SUBMUCOSA OF AN ATROPHIC INTESTINE.

(*Alum-carmine staining:* × 80.)

a, glandular layer reduced to a half of its normal thickness.
b, muscularis mucosæ.
c, submucosa.
d, outer muscular coat.
e, atrophy complete.

great size, repair is effected by granulation and cicatrization, or a chronic open ulcer is formed.

As regards **hyperplasia**, the various membranes comport themselves in different ways. Hyperplasia of the uterine mucous membrane is very common; in the bladder, œsophagus, and small intestine it is rare. The hyperplasia is manifested as a more or less extensive thickening of the membrane, or in the production of localized papillary, polypous, or fungous excrescences. These changes are most commonly met with in the uterus, stomach, colon, and nose.

The thickened or polypous membrane may be altogether normal in its apparent structure. But as the hyperplastic process is very frequently associated with some form of inflammation, the overgrown portions usually exhibit certain morbid alterations. The epithelium is often atrophied, the glands obliterated or transformed into cysts (Art. 422), while the fibrous elements are increased, and infiltrated with cells. In other instances the glands may be hypertrophied.

CHAPTER XLVI.

INFLAMMATORY AFFECTIONS.

419. The inflammations of the mucous membranes are the commonest of all affections, and they play a very considerable part in pathology. In by far the greater number of cases they are induced by noxious agencies acting on the external surface of the membrane; they are rarely due to noxious matters carried to it by the circulation. Thus cystitis, that is inflammation of the mucous membrane of the bladder, is often caused by the action of morbid or decomposed urine; intestinal inflammation by the ingestion of irritant substances; and bronchial inflammation by the inhalation of impure air. Symptomatic inflammations are met with chiefly in connection with certain general infective diseases.

The intensity, extent, and duration of the inflammations of the mucous membranes vary greatly in different cases; and a number of different forms are distinguished accordingly.

420. In **catarrhal inflammations,** as the name implies, the characteristic feature is a morbid increase of the secretion of the membrane. Hyperæmia is of course present, and often to a remarkable degree in the early stages, but the alteration in the nature and amount of the secretion is the distinguishing character.

The catarrhal secretion is furnished partly by the blood-vessels and partly by the epithelial cells. In the early stages the blood-vessels permit the extravasation of an abundant colorless or sometimes blood-stained liquid, containing a multitude of white corpuscles (Fig. 166, 1) interspersed with a few red ones. When the secretion consists essentially of this liquid exudation, we have what is called **serous catarrh.**

The liquid exudation from the blood-vessels is always mingled with secretions from the epithelial cells. These cells normally produce mucus from their protoplasmic contents—the cylindrical cells chiefly, but to some extent also the stratified pavement epithelial cells, like those of the bladder. The process may be well observed in the cells of the intestinal and bronchial epithelium; the so-called goblet-cells of these membranes being simply mucus-forming structures. In catarrh the production of mucus is much increased, the number of goblet-cells (Fig. 166, 6) becoming considerably greater than in normal conditions. Great quantities of glassy mucus are thus deposited on the membrane, or, as in the case of nasal catarrh, are cast off from its free surface. If the membrane con-

tains mucus-glands their secretion is simultaneously increased, and mingles with that of the lining epithelium.

At first the changes just described are the only ones, or at least the only ones that are obvious. Sooner or later however other changes set in, unless the inflammation speedily subsides and the membrane recovers. The epithelial cells begin to be shed, and the secretion is rendered turbid by their presence. These cells vary of course in appearance with the character of the membrane to which they belong. From cylindrical epithelium we get cylindrical cells (3), which are swollen and translucent or altogether in a state of mucoid degeneration (Art. 55). Goblet-cells (6), ciliated cells (5), squamous pavement cell (11, 12, 18), are all met

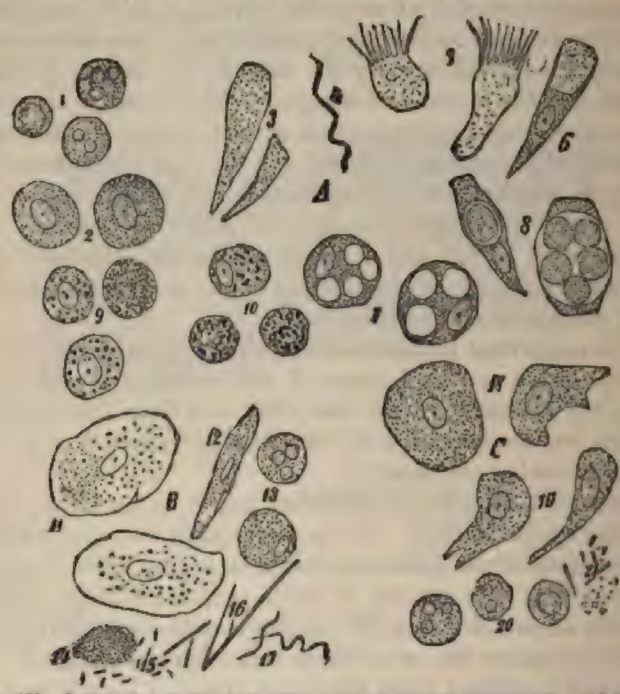


FIG. 166. CATARRHAL SECRETIONS FROM VARIOUS MUCOUS MEMBRANES. (× 400.)

A from cylindrical epithelium, *B* from the mouth, *C* from the bladder. 1, leucocytes (pus-corpuscles). 2, large leucocytes with clear nuclei from the nose. 3, mucoid cylindrical cells from the nose. 4, *Spirillum* from the nose. 5, mucoid ciliated cells from the nose. 6, globet-cell from the trachea. 7, leucocytes from the nose, containing masses of mucus. 8, epithelial cells from the nose, containing pus-corpuscles. 9, fatty cells from cases of chronic laryngeal and pharyngeal catarrh. 10, cells from sputum containing soot-pigment. 11 and 12, squamous epithelium from the mouth. 13, mucus-corpuscles. 14, micrococci. 15, *Bacterium termo* 16, *Leptothrix buccalis.* 17, *Spirochæta denticola.* 18, cells from the surface layer—and 19, from the deeper layers—of the bladder. 20, pus-corpuscles. 21, *Schizomycetes* or bacteria.

with in catarrhal secretions. Where the epithelium is stratified the polymorphous cells of the deeper layers (19) may be shed with the superficial cells. When the secretion thus contains a considerable proportion of shed epithelial cells we have what may be called **epithelial catarrh.**

In the later stages we may have not only an excessive desquamation of the epithelium, but also an abundant extravasation of leucocytes from the superficial blood-vessels. Many forms of catarrhal inflammation are thus characterized by an almost purulent secretion, and are described as **purulent catarrh.** The leucocytes may be small and uninuclear, or may appear multinuclear in consequence of the breaking-up of their nuclei into fragments (1, 13, 20). In recent cases they are often swollen and slimy-looking, and constitute the so-called mucus-corpuscles (13). Sometimes spherical cells are met with, which contain transparent globules of mucus in their interior (7); and the smaller leucocytes may at times penetrate into the substance of the degenerate and desquamated epithelial cells (8). Such cells have been mistaken for brood-cells. In chronic catarrhs some of the cells undergo fatty degeneration (9); while others contain particles of dust or soot (10) derived from without.

The components of the catarrhal secretions above referred to are such as come from the mucous membrane itself. Many extrinsic substances may however be found mingled with these. In catarrh of the bladder we often find crystalline deposits from the urine mixed with the mucous secretion; the secretion of intestinal catarrh is always mingled with matters derived from the food. Bacteria are also very frequently met with (4, 14, 15, 16, 17, 21), in the various forms of micrococci, bacilli, and spirilla. They are in part to be regarded as unimportant accidental impurities, in part as irritants inducing or maintaining inflammation. It is impossible at present to decide the part taken by the different forms.

421. Catarrhal inflammations of the mucous membrane are usually transient. The characteristic symptoms sooner or later disappear and complete restoration follows. Sometimes however the process becomes chronic, and then certain secondary changes are induced.

In addition to the alterations in the secretion and the epithelial cells already mentioned, a membrane affected with catarrh shows signs of cellular infiltration in the connective tissue of the mucosa and often also of the submucosa; and this infiltration is in some cases very considerable. When complete restoration takes place the infiltrated cells disappear either by migration to the surface, or by passing into the lymphatics, or by disintegration and absorption. Where the epithelium has been lost by desquamation repair is effected by multiplication of the remaining epithelial cells.

This result is however not invariable; the inflammation may become intensified so that the tissues perish over some considerable extent, or continuing to be of moderate intensity it may be unduly protracted, and so occasion extensive alteration in the tissues.

The intensification of the inflammatory process is manifested histologically as an increase of the cellular infiltration. Thus, for instance, in the colon the surface layers of the connective tissue separating the lieberkühnian crypts may be densely infiltrated with leucocytes (Fig. 167 *d*). The overlying epithelium is soon lost; that of the crypts per-

sists; but it is often loosened and separated from its basement tissue. In the later stages it also may be shed altogether and extruded from the crypts.

When the infiltration is extreme the tissue perishes by necrosis. Patches of various sizes die outright and are cast off with the pus which is secreted from the surface (*f*). In this way ulcers (*g*) are produced which may be large or small according to the extent of the initial necrosis. The lymph-follicles, in membranes that possess them, are often the chief seat of the inflammation and ulceration. Ulcers starting in them are known as **follicular ulcers.** When catarrh of a mucous membrane passes into ulceration the inflammatory infiltration usually extends far beyond the limits of the ulcer. Thus in dysenteric ulceration of the colon the submucosa (*e*) is infiltrated as well as the mucosa (d d_1).

422. When the inflammatory process is of long duration, a certain

FIG. 167. SECTION OF THE COLON FROM A CASE OF DYSENTERY.

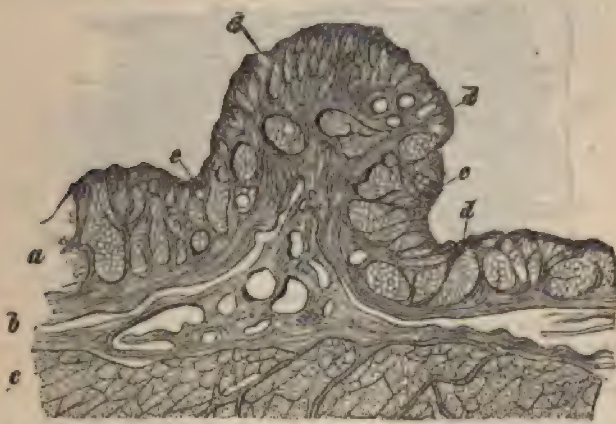
(*Hæmatoxylin staining*; × 25.)

a, mucosa.
b, submucosa.
c, muscular coat.
d, infiltration of the mucosa between the crypts.
d_1, infiltration beneath the crypts.
e, infiltration of the submucosa.
f, infiltration of the superficial glandular layers which are in process of desquamation.
g, ulcer with infiltrated floor.

amount of **fibrous hyperplasia** takes place, and that whether the process is accompanied by ulceration or not. In the former case the hyperplastic tissue often takes the form of papillomatous outgrowths from the borders of the ulcer, and these sometimes reach a remarkable size. Even where there is no ulceration similar papillomatous, warty, or cauliflower excrescences may be formed. In other cases the fibrous hyperplasia is more diffuse, giving rise merely to bands and unevennesses of the surface; but both forms are often found associated.

Thus after long-continued catarrh of the stomach the mucous memne has often a grayish tint and is rough with dense fibrous bands and ...ies, or it is beset with ridges and prominences which do not disappear ...en the organ is distended (Fig. 168). These prominences are at least ...part due to fibrous overgrowth (e).

When the membrane contains glands, the openings of some of them ...ome obstructed, and they are thus distended into **cysts.** Some of ... glands may be obliterated altogether by the destruction of their ...thelium. In other cases new glands are formed, or at least papillary ...growths covered with epithelium spring up from the walls of the ...ndular cysts. The growths thus produced, which depend much more ... fibrous than on glandular hyperplasia, often resemble tumors, and ...e been incorrectly described as adenomata (Art. 167). They occur ...efly in the stomach and uterus, and might appropriately be called ...**lammatory papillomata.**



... 168. ATROPHY OF THE GASTRIC GLANDS WITH FIBROUS HYPERPLASIA OF THE MUCOSA.

(*Hæmatoxylin staining:* × 10.)

...cosa.
...mucosa.'
...cular coat.
d, hyperplastic fibrous tissue.
e, gastric glands.

...n the membrane contains lymphadenoid tissue, this may likewise ... hyperplastic under the influence of long-continued catarrhal ...ation. The follicles are enlarged and project as rounded nodules ... mucous surface.

...**roupous inflammation.** When a mucous membrane is so ...at its epithelium is here and there partially destroyed, and at ...ime its blood-vessels are so damaged that an abundant exuda...ured out on the surface, coagulation of the latter may take ...e manner described in Art. 35. In this way a pale yellowish ... (Fig. 169 a) is formed on the surface consisting of fibrinous

filaments and granules beset with pus-corpuscles, or of shining homogeneous blocks (*c*) representing cells which have undergone coagulative necrosis. This **false membrane** is connected with the underlying structures by fibrinous threads, but it is usually loosely adherent, and can be readily stripped off disclosing the red hyperæmic mucous membrane beneath. An inflammation of this kind in which the surface exudations coagulate in a loosely-adherent false membrane is described as croupous. It implies a somewhat abundant extravasation of liquid and of cells, and the absence of such agencies as hinder coagulation. The epithelial cells are always more or less injured, being either necrotic or in process of degeneration and desquamation; but this injury of the cells need not precede the appearance of the inflammation. Inflammatory disturbance of the circulation may be the primary lesion, and the alteration of the epithelium secondary.

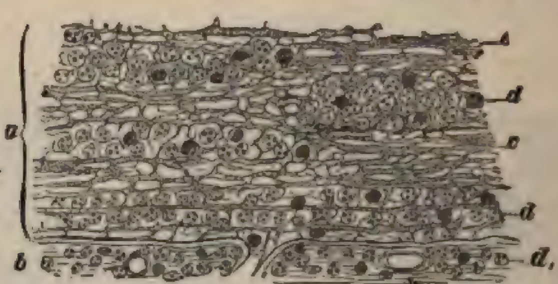


FIG. 169. CROUPOUS MEMBRANE FROM THE TRACHEA. (× 250.)

a, section through the false membrane.
b, upper layer of the mucous membrane, infiltrated with pus-corpuscles (d_1).
c, filaments and granules of fibrin.
d, pus-corpuscles.

The fibrous structures of the inflamed mucous membrane always contain liquid and cellular exudations. If the liquid lie in the larger lymph-spaces or in dilated lymphatics it also may coagulate and give rise to fibrous-looking clots, rarely to homogeneous and continuous masses. We might in such cases say that the cropous inflammation was deep or parenchymatous, as well as superficial in the ordinary sense.

Croupous inflammation occurs chiefly in the respiratory mucous membranes, rarely in the alimentary tract.

424. **Diphtheritic inflammation.** When a mucous membrane is injured in such a way that its epithelium dies without desquamation while its blood-vessels are damaged and pour out an abundant exudation, it sometimes happens that the dead epithelial cells become saturated with the exuded liquid and then pass into a peculiar condition of rigidity akin to coagulation. The seat of this change appears to the naked eye as a dull grayish raised patch surrounded by red and swollen mucous membrane (Fig. 170). The exudation is rich in albumen, and the trans-

ied cells take on the appearance of a kind of coarse mesh-work (*c*) ost or altogether devoid of nuclei. The subepithelial areolar tissue s beset with filaments of fibrin and leucocytes. Hæmorrhages (*f*) not uncommon. Inflammations of this kind, in which the tissue f coagulates into a solid mass, are called diphtheritic. When the osis and coagulation extend only to the epithelium we may speak of process as **superficial diphtheritis.**

As we said in speaking of the croupous membrane it is by no means ssary that the whole of the epithelium ultimately affected should sh at the outset; some part of it at least may perish secondarily, in equence of the inflammation.

Superficial diphtheritis occurs chiefly in the organs of the throat, but conjunctiva and the epithelium of the urogenital organs are also oc-

FIG. 170. SECTION THROUGH THE UVULA IN DIPHTHERITIS FAUCIUM.

(*Aniline-brown staining;* × 75.)

ial epithelium.
ial areolar tissue.
sed epithelium transformed into a rse mesh-work.
d, areolar tissue infiltrated with fibrin and leucocytes.
e, blood-vessels.
f, hæmorrhage.
g, heaps of micrococci.

attacked. The structure of the respiratory organs and the seems not to favor this form of inflammation. When their n perishes from any cause it is usually shed or dissolved away, pous false membrane is formed instead of the diphtheritic n.

ppears that croupous inflammation and what we have called superfi- ritis are very closely related. Speaking generally the distinctive the two processes are chiefly conditioned by the structure of the branes which they affect. Still it is convenient to assign distinctive n, and to reckon all cases in which the epithelium coagulates *en*

masse as diphtheritic. Necrosis and coagulation of the tissue are the distinguishing features of diphtheritic inflammation; whether it is superficial or deep its nature is the same, the mere seat is of secondary importance.

Inasmuch then as the croupous membrane consists essentially of coagulated exudation, croupous inflammation is at once distinguished from superficial diphtheritis. Nothing but confusion can result from speaking of the latter as pseudo-croup or pseudo-diphtheritis. True croupous inflammation may occur in mucous membranes that are normally covered with stratified epithelium, when the superficial cells have been destroyed and shed.

425. Deep or **parenchymatous diphtheritis** affects a greater extent of tissue than the superficial form. It is characterized by the coagulation not merely of the epithelium but also of the underlying connective tissue. The affected patch is swollen and assumes a whitish or grayish tint, the discoloration extending through the epithelium to the connective-tissue structures. The epithelium in some cases is lost altogether, and then the diphtheritic patch consists of dead connective tissue only (Fig. 171). The patch is turbid and granular in texture, or it may be

FIG. 171. SECTION OF THE UVULA FROM A CASE OF DIPHTHERITIS FAUCIUM.

(*The epithelium has been shed: aniline-brown staining:* × 100.)

a, micrococci.
b, submucous tissue changed into amorphous blocks.
c, extravasated leucocytes.
d, fibrinous exudation.
e, blood-vessels.
f, lymphatic vessel containing cells and fibrin.

homogeneous, or composed of amorphous hyaline blocks (*b*). The nuclei are always more or less completely lost. The small vessels (*e*) which permeate the patch show signs of a homogeneous transformation of their walls.

The dead tissue is separated from the living by a zone of cellular infiltration (*c*). Fibrinous filaments (*d*) are seen here and there through the mass. The lymphatics (*f*) in the neighborhood contain coagula and leucocytes.

Necrotic inflammation may attack any of the mucous membranes; it

is especially common as a result of infection of one kind or another. We are frequently able to demonstrate that it is associated with the invasion of the tissue by bacteria (*a*).

References on croupous and diphtheritic inflammation:—BRETONNEAU, *De la diphthérite* Paris 1826–27, *Arch. générales* 1855, *Memoirs on diphtheria* (New Syd. Soc.) 1859; VIRCHOW, *Handb. d. spec. Path. u. Ther.* I. Berlin 1854, and *Berl. klin. Woch.* 2, 1865; WAGNER, *Arch. d. Heilk.* VII., VIII., *Handb. d. allg. Path.*, *Ziemssen's Cyclop.* VII.; CORNIL and RANVIER, *Man. Path. Hist.* I. London 1882; WEIGERT, *Virch. Arch.* vols. 70, 72, 80, and Art. *Entzündung* in *Eulenburg's Realencyclop.*; ZAHN, *Beiträge z. path. Hist. d. Diphtheritis* Leipzig 1878; LEITZ, *Diphtherie u. Croup* Berlin 1877; OERTEL, *Ziemssen's Cyclop.* II.; SCHWENINGER, *Arbeiten a. d. path. Institute* Munich 1878; COHNHEIM, *Allg. Pathologie* I. Berlin 1881; HEUBNER, *Die experimentelle Diphtherie* Leipzig 1883.

426. The formation of the necrotic patch or slough is of course not the final stage of the diphtheritic process. The sloughs themselves act as irritants and set up inflammation around them. Superficial epithelial sloughs become in this way infiltrated with pus and so are loosened and cast off. The loss of substance is then made good by regenerative multiplication of the remaining epithelial cells. Larger and deeper sloughs may in like manner be separated by suppurative inflammation taking place around them, and the deficiency is then made up by the formation of a cicatrix, which in process of time may be covered over with new epithelium. But the process often maintains its destructive character for a considerable time, extending continually to greater depths, and often inducing intense purulent inflammation over a wide area around the initial lesion.

Sometimes the necrotic inflammation takes on a **gangrenous** character, that is to say micro-organisms penetrate the diseased tissues and set up in them septic or putrid decomposition. The affection is then much more grave, for the products of decomposition act as highly noxious irritants on the tissues that are still healthy. Definitive suppuration may however in this case also lead to the separation of the dead tissue from the living, and so allow the process of repair to begin.

427. **Phlegmonous inflammation.** In speaking of catarrh we said that the inflammatory process might become so intensified that it passed into the purulent form, that is to say into suppuration. In addition to this purulent catarrh we occasionally meet with a suppurative form of inflammation in which the exudation is purulent or fibrino-purulent, but is not like the former merely superficial. This form gives rise to diffuse purulent infiltration of the mucosa and submucosa, which may in consequence become enormously swollen and as it were saturated with pus. If the patient survives, large portions of the submucosa may break down and dissolve in the purulent exudation. This form corresponds to phlegmonous inflammation of the integument (cellulitis), and is also described as phlegmonous. It occurs in the mucous membranes

of the pharynx and stomach, and rarely elsewhere. It is due to some microparasitic infection.

When the affection is recent the tissues are everywhere infiltrated with liquid and cellular exudations and with pus-corpuscles. Here and there granular and fibrillated coagula are seen, and presently the infiltrated tissue and the extravasated cells become necrosed. The cells then look turbid and granular, lose their nuclei, and disappear; and the epithelium and connective tissue perish in like manner.

CHAPTER XLVII.

INFECTIVE GRANULOMATA AND TUMORS.

428. **Tuberculosis** of the mucous membranes is one of the commonest of all diseases. In post-mortem examination we generally meet with it in the form of tuberculous ulceration, but opportunities often occur for studying the process in its early stages. It begins as a cellular infiltration of the sub-epithelial tissue, which is either localized in definite nodules, or diffusely scattered with here and there slightly marked aggregations. If there are any lymph-follicles in the tissue the infiltrated cells tend to accumulate round them. The smallest nodules of all have often no very characteristic appearance, but they occasionally contain giant-cells. Caseation usually sets in early (*c*). The tubercu-

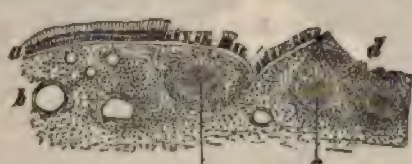


FIG. 172. TUBERCULOSIS OF THE BRONCHIAL MUCOUS MEMBRANE. (× 25.)

a, epithelium. *c*, tubercle.
b, infiltrated fibrous tissue of the mucosa. *d*, border of a small ulcer.

lous nodules, which at first project somewhat above the surface of the membrane, become thereupon white and opaque. Disintegration speedily follows; the sub-epithelial nodules break through the epithelium, and rounded or sinuous ulcers of various sizes (Fig. 172 *d* and 173 *h*) are formed. The floor and margins of such ulcers are infiltrated with cells, the surface portions being necrotic. Tubercles are often but not always found seated in the infiltrated zone.

In the mucous membrane of the bronchi and bladder the tuberculous growths do not attain any large size. In the larynx, glottis, and epiglottis the sub-epithelial granulomatous tissue may sprout into fungous growths resembling exactly the fungating granulomata of bone (Art. 121). The epithelium is thereby raised into warty excrescences, and when they break down more or less extensive ulcers are produced.

Tuberculous disease of the large and small intestine resembles that of the laryngeal mucous membrane, but the ulcerations are usually much larger. The tubercles (Fig. 173 i i_1) are seated chiefly in the submucosa;

the cellular infiltrations of the mucosa are less definitely aggregated. When the tubercles break down cavities are formed in the submucosa (h_1), which we may call **tuberculous abscesses,** and these gradually extend into and through the mucosa and ultimately form open ulcers on the surface (h).

The **tuberculous ulcer** when once formed usually advances by progressive disintegration of its infiltrated margins. The infiltration of cells and their aggregation into tubercles being very irregular in their course (Fig. 173), the process of disintegration is also irregular, and consequently the outline of a tuberculous ulcer of any great size is usually without any regularity. Its margins are often red and swollen and beset with grayish and yellowish nodules, or they may be but slightly swollen

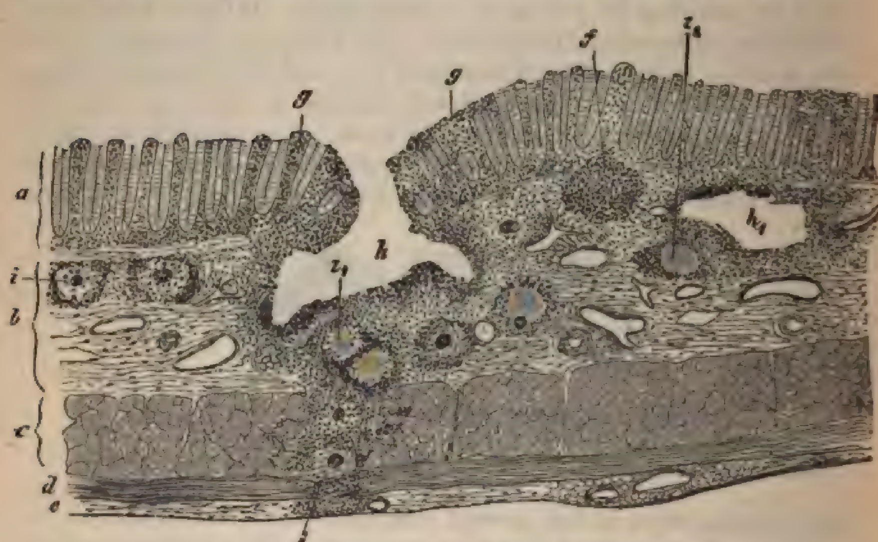


FIG. 173. TUBERCULOSIS OF THE LARGE INTESTINE.

(*Bismark-brown staining:* × 30.)

a, mucosa.
b, submucosa.
c, internal muscular coat.
d, external muscular coat.
e, serous coat.
f, solitary follicle.
g, cellular infiltration of the mucosa.
h, tuberculous ulcer.
h_1, tuberculous abscess.
i, recent tubercle.
i_1, caseous tubercle.

and sharply cut or even undermined. The floor is uneven and often beset with yellowish nodular deposits. Sometimes papillary outgrowths of considerable size arise from the margins and floor of the ulcer.

Complete repair very seldom takes place in a tuberculous ulcer. When it does it is by the separation and extrusion of the whole of the diseased tissue, healthy granulations springing up beneath it. From these cicatricial tissue is elaborated, which at length is covered over with epithelium growing in from the borders.

In most cases however the process advances steadily, and if death does not intervene a very extensive destruction of tissue is the result.

429. **Syphilis** gives rise to simple catarrhal inflammations of no great severity, and also to granulating ulcers analogous to those of tuberculosis. The ulcers begin as soft grayish-white elevations of the mucous membrane corresponding to the syphilitic condylomata of the skin. These look like hyperplastic follicular structures, but as a fact they do not start in the follicles. Cases do however occur in which the follicles are affected by syphilis; and then they become enlarged and speedily break down. The granulomatous syphilitic growths are seated chiefly in the mucosa and submucosa. When fully developed and about to break down they consist of simple cellular tissue exactly resembling granulation-tissue.

The first thing to appear is an eruption of small soft rounded nodules, which are often highly vascular. Sometimes (especially in the larynx) this is accompanied by the appearance of larger nodulated growths. These growths break down and form ulcers which continue to advance by progressive disintegration of their margins and floor. The diseased tissue is grayish or yellowish in tint. When the process comes to an end puckered scars and papillary excrescences are left. Syphilitic ulcers of this kind are met with chiefly in the mouth, pharynx, larynx, vagina, and rectum (Art. 435).

430. **Glanders** of the mucous membrane begins with the formation of small sub-epithelial nodules (Art. 135), which are generally larger than those of tuberculosis; sometimes indeed (as in the stomach) they are as large as a hazel-nut. Caseation, suppuration, and ulceration speedily ensue; the ulcers being covered with yellowish muddy-looking shreds of necrotic tissue, while their margins are red and hyperæmic. The foci of infection are usually numerous, new ones forming in contiguity to the old ones, and in this way, as successive ulcers coalesce, large irregular sinuous open sores are formed. They secrete a dirty creamy pus. When they heal they give rise to irregular puckered scars.

In horses the affection attacks chiefly the mucous membrane of the nose; it is rare to meet with it elsewhere, though sometimes the entire alimentary canal is beset with the characteristic nodules. Glanders of the mucous membrane in man is on the whole a rare affection.

Lupus affects the mucous membrane of the nose, mouth, pharynx, larynx, and perhaps the vagina; in course and appearance it exactly resembles the skin-affection (Arts. 132, 392).

Leprosy (Arts. 131, 392) appears as a nodular or diffuse infiltration of the mucous membrane of the mouth, pharynx, larynx, nose, and eyes. The nodules break down and give rise to leprous ulcerations.

431. The most important **tumors** of the mucous membranes are unquestionably adenoma and carcinoma. Other kinds are on the whole rarely met with, though cases are recorded of lipoma (in the intestine),

sarcoma (intestine, uterus), myxoma (vagina), fibroma (uterus, stomach), and lymphoma. The tumors which originate in the connective tissue usually take the form of rounded swellings projecting above the surface of the mucous membrane.

Adenoma (Arts. 167–169) appears in two different forms; either it is confined to the mucosa, or it extends into the submucosa and thence into the surrounding tissues and organs. The first form gives rise to polypous tumors whose general structure corresponds closely with that of the mucosa; that is to say though the glandular elements are larger, more numerous, and less regular than in the normal tissue, they exhibit the typical gland-structure characteristic of the membrane. They may most

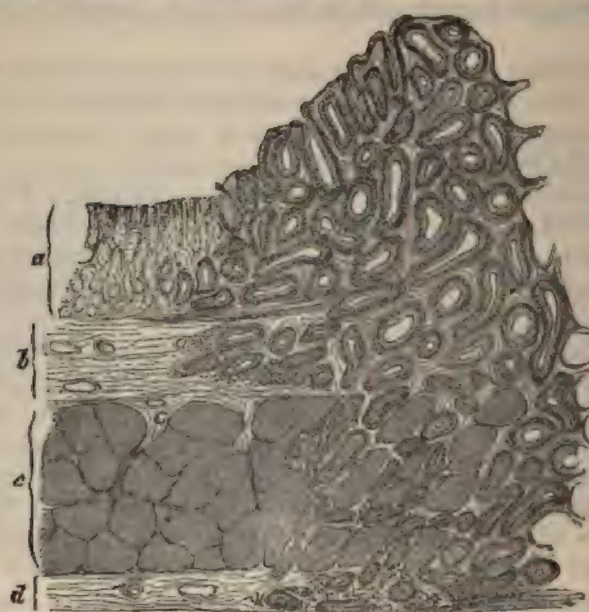


FIG. 174 *A*. DESTRUCTIVE ADENOMA OF THE STOMACH.
(*Hæmatoxylin staining*: × 25.)
a, mucosa. *b*, submucosa. *c*, muscular coat. *d*, serous coat.
e, adenomatous neoplasm starting from the mucosa and invading the other coats.

appropriately be described as **glandular hyperplasias** of the mucous membrane. The second form of adenoma, described as destructive adenoma, **adenocarcinoma**, or sometimes epithelioma, also agrees in structure with the glandular type, but its mode of growth and its tendency to invade the surrounding tissues distinguish it sharply from the other form.

Both adenocarcinoma and simple **carcinoma** take their origin in the lining epithelium of the surface, or in the epithelium of the glands. They form tumors that vary much in size and consistence. They both tend to infiltrate not only the mucosa but the submucosa and deeper

tissues, the infiltration resulting in the transformation and destruction of the invaded structures. Fig. 174 *A* illustrates this point very clearly. The neoplasm has started in the mucous glands of the stomach and thence invaded the several coats, altering and destroying their structure in its progress.

All cancers (adenocarcinomata and carcinomata) of the mucous membrane ultimately break down and ulcerate, giving rise to what are called cancerous ulcers. Blood-vessels are sometimes invaded and serious hæmorrhage may thus be caused. The cancerous infiltration advances steadily, and is closely followed by the ulceration ; in this way open sores of extraordinary size are produced. For example, cancerous ulceration of the uterus sometimes leads to frightful destruction of the pelvic and abdominal organs ; the greater part of the uterus, and the walls of the bladder, vagina, and rectum may be successively attacked and destroyed. Cancer of the intestine usually proves fatal before the destruction of tissue becomes very extensive.

It sometimes happens in cases of cancer of the mucous membrane that the greater part of the neoplastic tissue is itself destroyed by ulceration. The open wound which is left granulates and cicatrizes, giving rise to marked induration and contraction of the tissues. A true cancerous ulcer, open or cicatrized, may in such a case look exactly like a simple inflammatory ulcer or induration.

Carcinoma of the mucous membrane takes various forms ; sometimes it is soft and marrowy, and is then clinically described as encephaloid or medullary cancer ; in other cases it is firm and coarsely fibrous in structure ; in other cases again it is colloid or jelly-like.

SECTION VII.

THE ALIMENTARY TRACT.

CHAPTER XLVIII.

GENERAL CONSIDERATIONS.

2. The **alimentary canal** consists essentially of an epithelial tube, ı is furnished on its outer surface with certain auxiliary structures y of a muscular kind. The diseases of the alimentary canal are for the most part diseases of mucous membrane. Their pathology inly a special application of the general principles considered in the ection. In particular the causation of most of these diseases comes the description already set forth in general terms. They are due ule to the presence in the alimentary canal of substances which are noxious in themselves, or have undergone some abnormal decompo- after ingestion. It is not to be forgotten, however, that irritant rs may be conveyed to the intestinal tissues by the blood or lymph, hat morbid changes may be thus induced.

he different segments of the alimentary canal differ considerably in structure as well as in their functions. To these differences corre- l certain striking differences in the pathological phenomena they it. The forms of disease to which they are subject, the course a disease may run, and the textural changes it sets up, all differ in ifferent parts of the tract. In fact this single viscus furnishes us numerous and striking illustrations of the principle—that the special assumed by a disease depends not merely on the nature of the ori- ng cause, but also to a great extent on the structure of the affected , in other words on the anatomical predisposition of the tissues re involved.

CHAPTER XLIX.

THE MOUTH.

Inflammatory affections: stomatitis.

433. The **inflammations** of the mucous membrane of the mouth resemble in some points the inflammations of the skin, and in other points those of mucous membranes in general. Various forms are distinguished according to their intensity.

The slightest degree of inflammation is described as **erythema**. It is characterized by more or less intense redness of the surface, and either rapidly disappears or passes into the more severe form known as **catarrhal stomatitis.** In this form the surface is intensely red or livid, the secretion of the membrane is increased, and the epithelium desquamates. Over the surface of the lips, cheeks, and gums the redness and swelling are in general uniformly diffused, on the hard palate they may appear in streaks and patches. The papillæ of the tongue are most affected; some of them usually become markedly prominent, and so give the surface a rough tuberculated look.

When the inflammatory exudation is abundant, clear vesicles or blebs are sometimes formed on the tongue, lips, and cheeks, where the epithelial covering is thicker or tougher than elsewhere and prevents the free escape of the exuded liquid. But here, as in the external skin, the process of vesiculation is always accompanied by a certain amount of liquefaction of the deeper epithelial cells. As the vesicles break small ulcers covered with a whitish film of detritus may be formed in their place.

The mucous glands become swollen, giving rise to grayish or grayish-red elevations of the surface, surrounded by a reddened areola. When its excretory duct becomes obstructed with mucoid cells, the gland may be dilated into a tiny cyst by the retention of its secretion.

In recent acute catarrh of the mouth the catarrhal secretion contains comparatively few cells; in the later stages the proportion becomes increased. The cells are in part extravasated leucocytes, in part desquamated epithelial cells. If the latter remain on the surface, they may accumulate so as to form a whitish or discolored gray and brown deposit or '**fur**,' which in the case of the tongue may reach a considerable thickness. Fissures and cracks often appear on the surface of the lips and at the angles of the mouth, and these may exude liquid and become covered with crusts. They may pass by degrees into small ulcers.

Catarrhal stomatitis is generally the result of some mechanical or chemical irritation of the oral mucous membrane: when the irritation is local, like that caused by a carious tooth, the stomatitis is likewise local. But there are also many specific poisons that set up inflammation within the mouth. In measles a spotty or macular eruption appears, in scarlatina a punctate or diffuse scarlet eruption. In small-pox, chicken-pox, herpes, pemphigus, and in foot-and-mouth disease, there are eruptions of vesicles and pustules, which pass through the same stages as those of the skin (Art. 370).

Erysipelatous inflammation may extend from the skin to the mouth, or may actually begin in the mouth, causing dark or livid redness and much swelling and sometimes even vesiculation (Art. 375). The tongue is the part most affected, inasmuch as not only the mucosa but the intermuscular connective tissue become densely infiltrated with liquid and migratory cells.

Aphthous stomatitis is a peculiar form of the catarrhal inflammamation. It is distinguished by the appearance on the catarrhal mucous membrane of small whitish or slightly yellowish patches (*aphthæ*) from the size of a hemp-seed to that of a split-pea. The patches are isolated or grouped, and are most abundant over the tongue and lips. They are surrounded by a livid border, and may coalesce into larger patches or streaks, though these seldom reach any great size.

These aphthæ consist of a solid fibrinous exudation lying between the fibrous tissue and the epithelium (Bohn). The exudation may be reabsorbed, and the aphthæ then disappear. More commonly however the thin epithelial covering is broken through, the fibrinous film is exposed, and gradually separated and extruded by regenerative growth of the epithelium advancing beneath it from the margin. As the epithelium is reproduced simultaneously with the separation of the fibrin, no ulcers are in general produced; sometimes however suppuration is set up in the zone surrounding the aphthæ. The eruption occurs in successive crops and may thus be kept up for weeks.

Aphthous inflammation has been compared (Bohn) with impetiginous eczema of the skin (Art. 385). It occurs chiefly in children who are teething or otherwise subject to inflammatory affections of the mouth. It also occurs in connection with sore throat (angina), and with pneumonia, gastric catarrh, the acute exanthema, diphtheria, ague, whooping-cough, etc. It is rarely met with in adults, though it has been observed in women during menstruation, in pregnancy, and during the puerperal period. The affection is entirely unconnected with any invasion of fungi (Art. 436).

On croupous and diphtheritic stomatitis see Art. 443; on corrosive stomatitis see Art. 450.

The term **aphthæ** has not always been applied to the same affection. Hippocrates describes the white patches of 'thrush' (Art. 436) as aphthæ; and many

authors still use the term in this sense, while others apply it to various other affections of the mouth. Nowadays common usage is more strict, and the term is confined to the form of stomatitis spoken of in the text (BOHN). See BILLARD (*Maladies des enfants* Paris 1823), BOHN (*Die Mundkrankheiten d. Kinder* Leipzig 1866, and *Gerhardt's Handb. d. Kinderkranheiten* IV.).

The foot-and-mouth disease of cattle is sometimes communicated to man, the infection being generally conveyed by the use of uncooked milk from diseased animals. Small vesicles with whitish turbid contents appear on the mucous membrane of the mouth; they then rupture and leave behind dark-red slowly-healing erosions. See BOLLINGER (*Ziemssen's Cyclopædia* III.), PÜTZ (*Die Seuchen u. Herdekrankheiten* Stuttgart 1882), DEMME (*Bericht üb. d. Thätigkeit d. Kinderspitals* Berne 1882).

434. **Ulcerative stomatitis** is an affection which always starts from the alveolar margin of the gums (BOHN). It begins with redness, swelling, and loosening of the gums around the teeth. The alveolar margin becomes rounded and swollen, with blunt processes rising up between the teeth; hæmorrhage is not uncommon at this stage.

In the second stage the margin of the swollen gum becomes discolored, and the tissue softens and breaks down into a yellowish friable mass. Ulcers are thus formed, which rapidly deepen, the surface being overspread with shreds of softened tissue. The ulcerative process may extend directly to the contiguous parts of the cheeks and lips, and may work downward till it attacks the periosteum of the bony structures, leading to necrosis and the formation of sequestra.

The affection is usually acute, seldom chronic; children are especially liable to it, but adults do not escape. It attacks persons who are badly nourished or debilitated by disease, such as scrofulous disorders, intestinal complaints accompanied by exhausting discharges, typhoid, diabetes, or scurvy. Damp, cold, and impure air seem to favor its appearance.

Local irritation or injury may also lead to it, as in cases of chronic poisoning by mercury, phosphorus, lead, and copper. All of these substances if they repeatedly gain access to the mouth may cause ulcerative inflammation. The form which is due to long-continued phosphorus-poisoning is very apt to extend deeply into the tissues, and so give rise to periostitis and necrosis of the bones of the jaws.

Noma, *cancrum oris*, or 'water canker,' is an affection allied to ulcerative stomatitis, but of a much more serious character. It may begin as an ulcerative stomatitis or appear independently (BOHN). In the former case the disintegration of the tissue of the gums extends rapidly, and the tissue breaks down into a pulpy gangrenous or putrid mass. If the affection is not preceded by ulcerative stomatitis, the first symptom is the appearance of a livid swelling on the inner surface of the cheek near the angle of the mouth, accompanied generally by a free flow of foul saliva; a patch of grayish-yellow infiltration then appears, and this speedily breaks down and becomes gangrenous. Sometimes vesicles or blebs arise on the gangrenous surface. The disease goes on to attack the

outer skin of the cheek, giving rise first to a purplish spot on which a kind of blister appears. The spot then becomes black, and gangrene sets in and spreads. As a rule the surrounding tissue is highly œdematous.

The affection is generally confined to one side. Once the gangrene has begun the destructive process advances rapidly in all directions and may reach an astonishing extent. It is nearly always fatal. In rare cases the process comes spontaneously to a standstill, and the wound heals by granulation and cicatrization, resulting in more or less grave disfigurement of the face.

Noma is most frequent between the ages of two and twelve; it is rarely met with earlier or later. It attacks weakly or debilitated children, who are exposed to unhealthy conditions of various kinds.

Suppurative inflammation of the mucous membranes of the mouth and the parts underlying should be distinguished from ulcerative stomatitis and noma. It may affect any part, but appears most commonly in the tongue and gums. In the latter it frequently arises in connection with decayed teeth. The gum becomes red and swollen and presently pus forms beneath the surface; this is called a **gum-boil** or *parulis*. Suppurative inflammation of the tongue (**glossitis**) starts from a wound or ulcer, or from some acute inflammation like that due to erysipelatous infection. According to the way in which the inflammation starts, the whole tongue or a limited part of it becomes notably swollen, and presently appears more or less extensively infiltrated with pus. When the abscess so produced is evacuated, repair is effected by cicatrization.

References on ulcerative stomatitis and noma:—BOHN, *loc. cit.*; VON BRUNS, *Handb. d. operat. Chir.* vol. i. part 2, 1859; HIRSCH, *Historisch-geograph. Pathologie* II. 1864; GIERKE, *Jahrb. f. Kinderheilk.* (new series) I.

435. The infective granulomata described in Arts. 117–135 are all of them met with in the mucous membrane of the mouth.

Syphilis gives rise to primary, secondary, and tertiary lesions. Primary sores within the mouth resemble those of the skin (Art. 391). As secondary affections we have condylomata or mucous patches (Art. 379) on the lips and on the tongue, and also thickened opaline patches covered with milky-looking epithelial deposits and described as syphilitic psoriasis of the lips, tongue, or cheek; the latter resemble the superficial corrosions caused by applying nitrate of silver to the mucous membrane. Cracks, fissures, and ulcers due to syphilitic infection are frequently observed, especially about the tongue. In the tertiary stage gummata are formed, varying in size from that of a pea to that of a hazel-nut. They especially affect the tongue and are seated partly in the mucous membrane and partly in the muscular structures. When they break down they give rise to deep and spreading ulcerations. If the ulcers heal the scars are usually coarse and puckered. LANGENBECK states that can-

cers are apt to develop from gummatous nodes and scars (*Langenbeck's Arch.* XXVI.).

Lupus often extends from neighboring part to the mucous membrane of the mouth, and causes more or less extensive destruction of tissue (Art. 392).

Tuberculosis seldom attacks the mouth, but when it does it is chiefly the tongue which is affected. Tubercles are developed in the mucous membrane; the surrounding tissues become infiltrated and presently become caseous and break down. When such a caseous patch breaks through the surface layers, a tuberculous ulcer is produced. The edges and base of the tongue are favorite seats. The floor and margins of the ulcers are hard and densely infiltrated. When the tuberculous disease seizes on the muscular substance the greater part of the tongue may become studded with tubercles and infiltrated with granulation-cells.

With regard to **leprosy** and **glanders** see Arts. 131, 133, 392.

Parasitic affections.

436. The oral cavity is always infested by a multitude of vegetable microparasites, which gain entrance to it from without and find in it a fitting soil for their growth. Moulds, yeasts, and bacteria are all met with; of the latter micrococci and sarcinæ occur as well as bacilli and spirilla. Most of these fungi have no pathological significance; they are mere saprophytes subsisting on the remains of food and the dead or desquamated epithelium which lie decomposing in the mouth. Where cleanliness is not observed they may occasionally set up putrefactive decomposition and so cause irritation and inflammation.

Pathogenous organisms, however, often gain access to the mouth as well as these non-pathogenous forms. The **tuberculous bacillus** is constantly found in the sputa in cases of tuberculous phthisis, and in this way must occasionally lodge in the tissues of the mouth. And we have already pointed out that tuberculosis of the mouth does occur (Art. 435). The **ray-fungus** or *Actinomyces* (Arts. 134–135) attacks the tongue and jaws, producing the peculiar affection called actinomycosis (Fig. 174 *B*).

By way of a correction to the account of actinomycosis given in the first vol-ume (Arts. 134 and 135) we may here note that though ISRAEL was the first to ob-serve and describe the ray-fungus in the human subject, it was PONFICK who first recognized the true nature of the disease, and declared it (*Berl. klin. Woch.* 1879, *Breslau ärztl. Zeitschr.* May 9, 1879) to be identical with the cattle-disease previously described by BOLLINGER. PONFICK was also the first to demonstrate the genesis of the disease by means of his inoculation experiments.

Measles, scarlatina, erysipelas, small-pox, diphtheria, etc., all give rise to inflammatory conditions of the mouth; and as we regard these diseases as due to microparasites, we must assume that the corresponding pathogenous organisms gain acess to the tissues of the mouth.

Saccharomyces albicans (REESS), *muguet*, or **thrush-fungus** is a

special parasite of the mouth ; it has hitherto generally been referred to as *Oïdium albicans*. It is one of the *Blastomycetes* or yeasts, and is therefore akin to if not identical with *Mycoderma vini* or *Saccharomyces cerevisiæ* (Art. 224). As it occurs in the mouth it assumes the form of rounded or oval glistening cells and delicate filaments. Outside the body it may be cultivated in sugary or starchy liquids, and then produces round or oval cells, seldom filaments. When it grows in the mouth it gives rise to minute whitish slightly raised specks on the mucous membrane. These may be sparsely scattered or aggregated into groups on the inner surface of the lips and on the tongue. As they grow and multiply they coalesce into whitish or discolored films. After a time the film is cast off, the surface

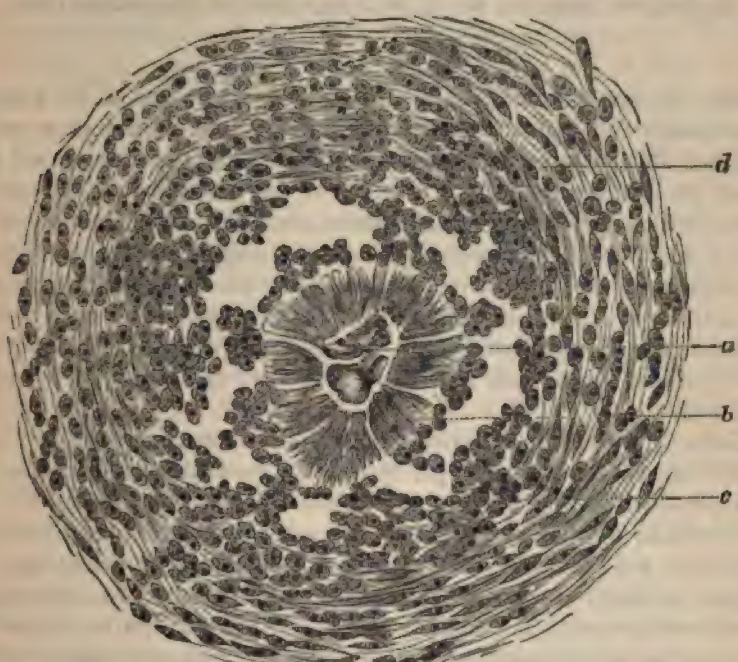


FIG. 174 *B*. NODULE CONTAINING *ACTINOMYCES* FROM THE TONGUE OF A COW.

(*After SIMS WOODHEAD: Stained with Spiller's blue:* × 300.)

a, central core (? mycelium).
b, radiating club-shaped bodies (? conidia).
c, epithelioid cells in the granulomatous nodule.
d, formative cells and new fibrous tissue.

beneath appearing red and sometimes eroded. The thrush-film may reappear on the same spot, and the affection may advance gradually till it reaches the pharynx and sometimes even the œsophagus.

The fungus grows mainly in the middle layers of the stratified epithelium. The upper layers are thereby raised and shed. The filaments and spores are usually thrust between the cells, though sometimes they penetrate the cell-substance and multiply within it. From the middle layers the fungus may penetrate into the deeper layers and ultimately reach the

fibrous structures. According to WAGNER and BUHL it may even penetrate the blood-vessels. As it grows downwards it sets up inflammation in the deeper tissues.

Young children are especially liable to thrush. The fungus may develop in the perfectly healthy mucous membrane of the new-born infant. Its growth is favored by the use of cows' milk and starchy foods, and by imperfect cleansing of the infant's mouth. Among adults it is nearly always in case of great weakness or wasting due to diseases like typhoid, septicæmia, phthisis, etc., that thrush makes its appearance.

References: Art. 224; REUBOLD, *Virch. Arch.* vol. 7; BURCKHARDT, *Charité-Annalen* XII. (1864); GRAWITZ, *Virch. Arch.* vols. 70, 73; REESS, *Phys.-med. Gesell. zu Erlangen* 1877–78; BOHN, *loc. cit.*; E. WAGNER, *Jahrb. f. Kinderheilk.* 1868.

Hypertrophy and Atrophy.

437. The epithelium of the mouth, and especially that of the tongue, is continually being shed and continually renewed by regenerative multiplication. Whenever, as in catarrhal affections, the growth of new epithelium is increased, or the removal of the desquamated cells is impeded, whitish accumulations or deposits are formed on the surface of the mucous membrane. These deposits are often augmented by the remains of food, and by rapidly-growing fungous parasites which settle in them, and in this way a continuous film or fur is produced. This may assume the most various tints according to the food used, and if the mouth be kept open may dry up into crusts and irregular flakes separated by cracks and fissures.

Under long-continued irritation, such as is caused by the constant slight friction of the tobacco-pipe, by fungous growths, or by syphilis, the oral epithelium may pass into a morbid condition resembling cornification. White streaks and patches on the tongue and cheeks are thus produced, which have received very various names. The milky opaline patches (*plaques opalines*) of syphilis have already been referred to (Art. 435). SCHWIMMER proposes the name of **leukoplakia** for the non-syphilitic white patches which sometimes follow upon erythematous inflammation. Others speak of such patches, which are characterized by thickening, cornification, and desquamation of the epithelium, as **lingual psoriasis** or ichthyosis. There seems some ground for believing that leukoplakia is in certain cases at least a precursor of epithelioma of the tongue (HULKE, NELIGAN, BARKER). DESSOIR describes a certain dark discoloration of the tongue due to accumulations of spores, dead epithelium, and accidental impurities, as *langue noire* or **glossophytia.** A hyperplastic condition of the epithelium, in which hair-like epithelial processes rise from the tips of the lingual papillæ, has been described as 'hairy tongue.'

Hyperplasia of the connective tissue of the oral mucous membrane and the adjoining structures is due either to some chronic inflammatory

process, or to conditions that are congenital or developed in early infancy.

Inflammatory hyperplasia is most commonly met with in connection with the gums. It gives rise to circumscribed tumor-like thickenings, which usually retain for long the aspect and texture of granulation-tissue, and may therefore be described as granulomatous. Chronic inflammation of the tongue generally leads to fibrous induration and deformity, the muscular tissue becoming degenerate and atrophied.

Congenital and infantile hyperplasia affects chiefly the lips (**macrocheilia**) and tongue (**macroglossia**). The lips may be so thickened as to look like great unwieldy tumors: the tongue may outgrow the capacity of the mouth to hold it, and it may thus press the teeth outwards and protrude from the mouth (*prolapsus linguæ*, glossocele). The protruded part is usually dried up and fissured, and ulcers form at the points where it is in contact with the teeth. In the congenital form the enlargement is seldom very great at birth, but it rapidly increases in the first few months of life. The affection is frequently met with in cretins and idiots.

The enlargement of the tongue and lips is due either to an overgrowth of all the constituent tissues or of the fibrous tissue only, or to the development of neoplastic tissue. The overgrowth may be local or general: in the former case isolated nodes and tuberosities are produced.

In the fibrous form the muscular fibres are generally diminished in number; the fibrous tissue may be dense and firm or soft and cellular, and it is here and there infiltrated with leucocytes. The infiltration is most marked when the protruded portion of the tongue is fissured and ulcerated, and so subject to intercurrent inflammation. The lymphatics of the hyperplastic fibrous tissue are nearly always dilated (Art. 438).

Of the atrophies and degenerations to which the tissues of the mouth are liable those that affect the tongue are the only ones of any great importance, and of these the most striking are those that affect its muscular substance. Simple atrophy (Art. 46), fatty degeneration (Art. 50), and waxy degeneration (Art. 38) of the lingual muscles have all been described. They depend on local disorders of nutrition due to inflammatory conditions, or on neurotic disturbance in connection with disease of the hypoglossal nerve and its nucleus in the medulla oblongata.

Among the degenerative affections of the fibrous tissues amyloid change must be specially mentioned. It attacks the intermuscular fibrous tissue as well as that of the mucous membrane, and gives rise to isolated nodes or nodules, or (in the tongue) to a uniform lardaceous transformation. The muscles and mucous glands atrophy and disappear when surrounded by the amyloid substance.

Atrophy of the gums and the alveolar parts of the jaws is apt to follow upon loss of the teeth, and is especially notable in advanced age.

References on macroglossia:—Arts. 615, 438; WEBER, *Virch. Arch.* vol. 7, 16

Pitha u. Billroth's Handb. d. Chir. VI.; VIRCHOW, *Die krankh. Geschwülste* III.; ARNSTEIN, *Virch. Arch.* vol. 54; HUMPHRY, *Med. chir. Trans.* XXXVI. (1853); ARNOTT, *Trans. Path. Soc.* 1872; MAAS, *Arch. f. klin. Chir.* XIII.; WEGNER, *ibid.* XX.; CLARKE, *Diseases of the tongue* London 1873; VARIOT, *Journ. de l'anat. et de la physiol.* 1880; POSTER, *Jahrb. f. Kinderheilk.* XVIII. (1882); BARKER, *Holmes's Syst. of Surgery* II. London 1883.

On hyperplasia of the epithelium:—CLARKE, *Practitioner* Aug. 1874, *Brit. Med. Journ.* 1, 1874; SCHWIMMER, *Vierteljahrs. f. Derm. u. Syph.* V (1878); VOGEL, *Ziemssen's Cyclop.* VII.; KLEBS, *Arch. f. exp. Path.* V.; NEDOPIL, *Arch. f. klin. Chir.* XX.; HULKE, *Trans. Clin. Soc.* 1869; NELIGAN, *Dublin Quart. J. Med. Science* 1862; DEBOVE, *Le psoriasis buccal* Paris 1873; MAURIAC, *De la psoriasis de la langue et de la muqueuse buccale, Union méd.* 1873–74; R. WEIR, *Ichthyosis of the tongue, New York Med. Journ.* March 1875; TRÉLAT, *Bull. Soc. Chir.* 1875; *Trans. internat. med. congress* vol. III. London 1881; DESSOIR, *De la langue noire* Paris 1878; BARKER, *Holmes's Syst. of Surgery* II. 1883.

On amyloid change see ZIEGLER, *Virch. Arch.* vol. 65.

Tumors and Cysts.

438. The most important of the tumors affecting the mouth in the early years of life are the angiomata and lymphangiomata. **Angiomata** are met with chiefly about the lips, appearing as dark-red or livid slightly raised patches. **Lymphangiomata** occur in or about the tongue. Some of the tissue-changes included under the name of macroglossia are due to lymphangiomatous growths.

In Art. 437 we mentioned that the hyperplastic fibrous tissues in the tongue and lips generally contain dilated lymphatics. Cases often occur in which such lymphatics constitute the greater part of the substance of the tongue. The entire tongue—muscles, mucous membrane, and papillæ—may be transformed into a kind of fine-meshed sponge or honeycomb. The spaces and meshes contain lymph, the septa between consist of delicate fibrous tissue interspersed with a few scattered muscular fibres. The fibrous tissue may or may not be highly cellular. In the former case it contains patches of lymphadenoid tissue; the neoplasm is then in fact a combination of lymphangioma and lymphadenoma. In other cases the tissue contains an extraordinary amount of fat, the tumor being then most fitly described as lymphangio-lipoma. The dilated lymph-spaces are usually small, but sometimes they become distended into globular cysts, from the size of a pea to that of a cherry (**cystic hygroma**).

The lymphangiomatous growth is often confined to the tongue proper, but it may extend to the neighboring parts, or new foci may appear in the tissues of the root of the tongue. It would seem that the largest cysts are met with in the latter situation. From the root of the tongue the growth may extend in various directions, occasionally passing down towards the pharynx or upwards to the palatal structures.

Of the other congenital or infantile growths within the mouth we may mention the teratomata (Arts. 13, 178). Lipoma, fibroma, myxoma,

and sarcoma also occur; they form tumors which vary much in size and seat.

Of the tumors which develop in later life sarcoma and carcinoma are the most notable. **Sarcoma** mainly affects the gums (sarcomatous epulis), and as a rule starts in the deeper-lying structures like the periosteum or bone-marrow. It forms rounded tuberous growths, usually somewhat firm in consistence. When it starts in bone it contains bony trabeculæ in its substance (osteo-sarcoma, Art. 165), or sometimes giant-cells (myeloid sarcoma, Art. 159).

Carcinoma (in the form of **epithelioma**) attacks the lips, tongue, and gums. It begins as a small nodule, or a circumscribed hard grayish infiltration of the mucous membrane. Presently this becomes a palpable node projecting above the surface. The infiltrated tissue ulcerates, and around the ulcer the cancerous infiltration spreads more or less rapidly. If the diseased tissue is not removed, the cancerous ulcer may reach an astonishing size, especially in the case of the tongue and the gums. Adenoma of the mucous glands is a rarer form of tumor; it gives rise to circumscribed nodular growths.

References on lymphangioma of the mouth :—Art. 437 ; BILLROTH, *Beiträge z. path. Histologie* Berlin 1858 ; VIRCHOW, *Virch. Arch.* vol. 7 ; MAAS, *Arch. f. klin. Chir.* XIII.; VON WINIWARTER, *Arch. f. klin. Chir.* XVI.; GIES, *ibid.* XV. ; WEGNER, *ibid.* XX.; ARNSTEIN, *Virch. Arch.* vol. 54.

On lipoma of the tongue see WEBER (*Pitha u. Billroth's Handb. d. Chir.* VI.), GOSSELIN (*Paris médical* 20, 1881). On epithelioma see BARKER (*Holmes's Syst. of Surgery* II. London 1883).

439. As we pointed out in article 433, when the mucous glands are chronically inflamed they may become distended with accumulated secretion, and thus form small cysts of retention. Dilated lymphatics may likewise give rise to cysts, known as cystic hygromata (Art. 438). In addition to these varieties there are a number of other cystic structures, which occur in the mouth in various situations, more especially in or around the frænum of the tongue. These are referred to as cases of **ranula,** and have long been objects of considerable surgical interest. Notwithstanding this the manner in which they arise has only recently received a satisfactory explanation. VON RECKLINGHAUSEN has shown by careful anatomical investigations that the true or classical ranula is in fact a cystic dilatation of one of the main ducts of the glands of Nuhn and Blandin, two small mucous glands situated beneath the tip of the tongue. The duct is obstructed probably by inflammatory changes either within or around it, and the part behind the obstruction (which need not be complete) becomes distended with the secretion poured out by the gland-cells.

The contents of the ranula consist of a clear viscid or ropy mucous liquid, resembling the white of an egg; it may be quite colorless or stained

pale yellow or brown or pink. It contains no saliva. The cyst itself is usually globular or ovoid and lies close by the frænum.

Besides this form of ranula (the typical form), there are other cysts which are loosely classed with it. Wharton's duct, leading from the submaxillary gland, may be distended into a cyst. The cyst in this case is usually fusiform or cylindrical, though at times it becomes more distinctly globular. The occlusion of the duct is in general due to inflammation or to the formation of salivary concretions or calculi.

The ducts of the sublingual glands (ducts of Rivini and Bartholin) may also become distended into cysts lying beneath the tongue; and dermoid cysts are met with in the same situation. According to ROSER congenital cysts of the neck (Art. 8) may be displaced inwards so as to lie beneath the tongue, and sometimes simulate ranulæ. They often contain sebaceous matters.

Cysts occur in other situations, but much less frequently. Thus they are found at times in the muscular substance of the tongue and in the mucous membrane of its base. Such cysts are usually small, but now and then they attain a very considerable size (BOCHDALEK, LOTZBECK, HAMMERICH). They are due to the dilatation of the glands that occur at the base and around the root of the tongue.

The mucous glands of the lips may in like manner be transformed into cysts, which vary from the size of a pea to that of a hazel-nut.

The origin of ranula, as we have said, has been recently investigated with great care by VON RECKLINGHAUSEN (*Virch. Arch.* vol. 84). He reviews critically the various observations and theories already published, and describes the results of his own work on the subject. The classical ranula he proves to be due to the dilatation of the duct of the mucous glands at the tip of the tongue. He rejects the suggestion of FLEISCHMANN that it originates from a mucous bursa lying on the surface of the genio-glossus muscle. This bursa has been sought for in vain by various investigators; and moreover the true ranula always possesses a well-developed cylindrical epithelium.

BOCHDALEK (*Oesterr. Zeitschr. f. prak. Heilk.* XII. 1866), LOTZBECK (*Memorabilien* XV. 1870), and HAMMERICH, *Ueb. Schleimcysten d. Zungenwurzel* Würzburg 1877) have written on the cysts that are found at the base of the tongue. According to VIRCHOW, REUBOLD, BOHN (*Die Mundkrankh. d. Kinder* Leipzig 1866), DENIS, BILLARD, and others, in most infants the mucous membrane of the palate (in the neighborhood of the raphe and anteriorly) is more or less beset with white miliary nodules of various sizes. They are developed in the second half of fœtal life, and are due to an accumulation of epithelial cells in the mucous glands of the hard palate. They may fairly be described as milium or comedones of the mucous membrane (Art. 404).

Changes affecting the teeth.

440. By far the most important morbid change affecting the teeth is that known as **caries**, a gradually progressive disintegration of the enamel and dentine.

First of all an opaque white spot (which may sometimes be discolored

green or black) appears on the transparent enamel. Here the prisms of the enamel are loosened and to some extent broken down. Then by degrees the dentine is attacked, and once attacked it usually disintegrates very rapidly. Decalcification of the dental tissue precedes the carious disintegration.

In the advancing margin of the diseased area the tubules of the dentine appear to be widened (KLEBS, LEBER, and ROTTENSTEIN) and surrounded by bright rings. Presently the tubules are seen to contain a granular mass, which turns blue when treated with iodine and increases in bulk at the expense of the bright rings. This mass is found to consist of micrococci and bacilli. According to KLEBS it is they that are the destroyers of the dental tissue, inasmuch as they have the power of decalcifying it. They are enabled to penetrate the substance of the teeth by the accidental formation of cracks or flaws in the enamel.

KLEBS has also shown that the mortar-like 'tartar' which often covers the teeth contains multitudes of micrococci and bacilli mingled with calcareous particles. He maintains that the organisms are able to precipitate calcium-salts from the nutrient materials they assimilate.

A very common result of caries is inflammation of the pulp or of the alveolar periosteum. The irritants which directly induce it are perhaps the bacteria which are present in the disintegrated dental substance, and set up septic decomposition around them.

The inflammation of the pulp and periosteum may pass into suppuration. In this case the surface of the gum in the neighborhood of the diseased tooth is red and swollen (**gum-boil** or *parulis*), and presently suppuration sets in and extends to the deeper tissue of the gum, forming an **alveolar abscess.** This breaks externally, and if the suppurative process around the root of the tooth continues, we may have formed an alveolar sinus or fistula.

Sometimes the inflammation extends beyond the region of the root of the tooth and gives rise to an extensive periostitis of the jaw. In this way large abscesses are sometimes formed, and necrosis of a portion of the jaw-bone may result.

References on dental caries:—KLENKE, *Die Verderbniss der Zähne* Leipzig 1850; NEUMANN, *Arch. f. klin. Chir.* VI.; LEBER and ROTTENSTEIN, *Untersuch. üb. d. Caries d. Zähne* Berlin 1867; WEDL, *Pathologie d. Zähne* Leipzig 1870; KLEBS, *Arch. f. exp. Path.* V., Article *Leptothrix buccalis* in *Realencyclop. d. gesammten Heilkunde;* COLEMAN, *Dental surgery and pathology* London 1881; Discussion, *Trans. internat. med. congress* III. London 1881.

According to MILLER (*Cent. f. d. med. Wiss.* 13, 1882, *Arch. f. exp. Path.* XVI.) the bacteria present in the mouth set up acid fermentations, and the acid produced decalcifies the dental tissues. Thereupon micrococci and bacilli penetrate the dentine and set up putrefactive decomposition in the decalcified tissue.

441. **Tumors** arising from or connected with the teeth are of two chief kinds. The one is spoken of as dental osteoma, the other as

odontoma. **Dental osteoma** or exostosis consists of a diffuse or somewhat circumscribed thickening of the *crusta petrosa* or cement; and ought indeed scarcely to be reckoned among the tumors, as it is rather of the nature of an inflammatory hyperplasia. Very few cases of true **odontoma** have been described. So far as can be made out the small tumors so named (composed of dentine and enamel) arise from the pulp of the tooth in the early stages of its growth. Odontoma cannot be developed when the tooth is mature.

Fibroma, myxoma, and sarcoma may in rare cases be developed from the pulp as the tooth is being formed. Such growths are however much more commonly derived from the periosteum of the dental follicle, the alveolar process of the jaw, the bone-marrow, or the gum itself. These tumors, which arise close to the teeth or actually from their sockets, are included under the surgical term **epulis.** Some of them start in inflammatory granulation-tissue, but most are really sarcomatous (Art. 438).

Cysts of the jaws may be produced by the morbid dilatation of the dental follicles. The cysts are seated on the alveolar ridge, and sometimes reach a very large size, some as large as an apple and larger having been described. Their contents are liquid, and occasionally rudimentary teeth are found in them **(dentigerous cysts).**

References:—VIRCHOW, *Die krankhaften Geschwülste* II. (1864–65); MAGITOT, *Mémoire sur les kystes des mâchoires* Paris 1872; USKOFF, *Odontom d. Unterkiefers, Virch. Arch.* vol. 85; SALTER, *Holmes's Syst. of Surgery* II. London 1883; EVE, *Brit. Med. Journ.* 1, 1883.

HUTCHINSON (*Lond. Hosp. Rep.* II., 1865; *Trans. Path. Soc.* 1858–59, and *Clinical Surgery* XI. London 1878) has pointed out that the permanent incisors, and especially the upper central incisors, of children suffering from congenital syphilis often undergo a peculiar arrest of development. They are either altogether stunted, or as they emerge from the gum their sides instead of being parallel converge, while the cutting edge is concave. After a time, the dentine being exposed, the cutting edge becomes deeply notched; and when the tooth is full-grown it appears pointed or peg-shaped, with the crescentic notch truncating its apex, so to speak. The cause of this deformity is said to be a specific alveolar stomatitis during infancy (BÄUMLER, *Ziemssen's Cyclop.* III.).

CHAPTER L.

THE THROAT.

442. The mucous membrane of the throat (including in the term the soft palate, tonsils, and pharnyx) resembles that of the mouth in structure; it contains, however, a large amount of lymphadenoid tissue, which at various points is aggregated into nodules or follicles. In the tonsils especially this tissue is very abundant. According to Stöhr (*Biolog. Centralblatt* 1882) lymphoid cells are continually migrating from the lymphadenoid tissue to the free surface.

The disorders of the back of the mouth and pharynx correspond with those of the mouth generally, and many of them are indeed but partial manifestations or results of the latter. Certain forms of inflammation and certain new growths are however confined to the soft palate, tonsils, and pharynx, or at least produce in them their most characteristic symptoms.

Inflammation of the throat (referred to generally as **angina** or **pharyngitis**) may be due to local irritation, or to some general affection like measles, scarlatina, or small-pox. The catarrhal varieties give rise to redness and swelling, which may be diffused or disposed in irregular streaks and patches. The mucous membrane at the same time pours out a slimy or purulent secretion, which often forms a film or coating on the surface. In some of the inflammatory affections (such as that which accompanies small-pox or herpes labialis) vesicles are formed; these speedily rupture, and leave small erosions of the surface (*angina vesiculosa*). Often too, especially in children, the inflamed membrane is beset or overlaid with white patches of thrush (Art. 436). The lymphadenoid follicles are sometimes the parts chiefly affected. The solitary follicles of the pharynx and the serous glands at the back of the tongue swell up and project above the surface, and the tonsils are likewise enlarged (*angina tonsillaris*). If the swollen follicles break down small erosions or ulcers may be left (follicular ulceration). In chronic catarrhal conditions these changes in the follicles and tonsils may become very marked *angina* or *pharyngitis granulosa*). At the same time the mucous membrane, especially that of the uvula, becomes thickened; and the mucous glands become hypertrophied or distended, and project above the surface like small granulations. Accumulations of shed epithelium and pus-corpuscles col-

lect in the crypts of the enlarged tonsils, forming gray or yellowish plugs which occasionally become calcified. The tonsils may also become permanently enlarged as a result of chronic or often-repeated inflammation; in other cases they become atrophied or shrunken. When they are enlarged the chief seat of hyperplasia is the lymphadenoid tissue, which appears more diffused and less markedly aggregated into follicles than is normal. When they shrink it is the lymphadenoid tissue which disappears, its place being partly taken by ordinary fibrous tissue. Inflammation of the tonsils is apt to issue in the formation of small **tonsillar abscesses,** which break through the surface and evacuate their contents. The site of such an abscess is afterwards marked by a cicatrix.

443. One of the most important forms of inflammation to which the throat is liable is the **diphtheritic inflammation,** most familiarly known in connection with diphtheria.

As we have have already seen (Arts. 424–426), diphtheritic inflammation of a mucous membrane is associated with the necrosis of the epithelial layers only (superficial form), or of the epithelial and fibrous layers together (parenchymatous form).

In the pharynx the process begins with the formation of small round grayish filmy patches on a red and swollen base. The grayish film is at first thin and soft, but presently it becomes thicker and more yellowish, or if hæmorrhage takes place it becomes brown or black. The patches are sometimes few and isolated, or numerous and confluent, in which case they often form large dense masses or false membranes. At first these patches or masses are closely adherent to the underlying tissue, afterwards they are loosened and can readily be removed or are cast off spontaneously. Often the underlying surface of the mucous membrane appears to be intact; it is reddened but there is no perceptible loss of substance: this is the case in superficial diphtheritis. In other cases a visible erosion or ulcer remains when the false membrane is removed: this indicates deep or parenchymatous diphtheritis. The floor of the ulcer is red or dirty gray, the latter showing that the necrotic inflammation has extended still deeper into the mucous membrane.

The seat of the diphtheritic patches varies much in different cases, as may be observed in the living patient as well as *post mortem*. Sometimes the tonsils are the parts most affected, in other cases the palate and uvula, and often enough the epiglottis and the entrance to the larynx.

In addition to the formation of these patches there is always a certain amount of œdematous swelling of the tissues, which in the case of the tonsils and the parts around the glottis frequently becomes extremely marked.

If the patient survives repair takes place by the extrusion of the false membranes, regeneration of the necrosed parts, and re-absorption of the exudation. If the necrosis has extended deeply cicatrices may be formed. Now and then the affection takes a more dangerous turn,

gangrene setting in and causing very rapid and extensive destruction of the tissues.

A certain amount of croupous exudation very often accompanies the development of the diphtheritic membranes. Some of the gray or yellowish patches may consist simply of coagulated exudation, such as characterizes simple croupous inflammation. These patches are apt to be formed at spots where the epithelium has been stripped off.

444. Pharyngeal diphtheritis may be the result of various noxious agencies. It can be produced in animals by the action of certain corrosive substances properly applied to the mucous membrane. In man it is most commonly observed in connection with various infective diseases, such as scarlatina, measles, typhoid, small-pox, and diphtheria. It is the characteristic symptom of the latter.

Diphtheria is an infective disease, met with chiefly in children. The virus enters the system usually by the mucous membrane of the pharynx, and it first of all sets up local inflammatory changes there. The changes may be simply of the nature of catarrh, or they may be more intense and more dangerous. In by far the greater number of cases the various processes of diphtheritic inflammation are induced. But in many instances the epithelium is simply shed, and circumscribed yellowish typically croupous false membranes are formed from the coagulated fibrinous exudation. Gangrene is a rarer complication. The mucous membrane of the respiratory organs—larynx, trachea, and bronchi—is usually affected at the same time as that of the throat. Where the epithelium is cylindrical the inflammation is generally of the croupous type.

It seems now highly probable that diphtheria is due to an invasion of micrococci. When the affected epithelia are examined in the early stages of the disorder, we find in and upon the inflamed spots heaps and clusters of micrococci (Fig. 170 *g* and Fig. 171 *a*) such as do not normally occur in the mouth or throat. These are regarded as the virus of the disease, and they are supposed to affect the system in general through the vessels of the pharynx.

We have not here space to describe in detail the various controversies that have arisen as to the nature of the virus of diphtheria. The most important references have been given in Art. 204. HEUBNER recently investigated the subject of scarlatinal diphtheritis (*Jahrbuch der Kinderheilk.* new series XIV.) and compared it with the diphtherial affection. He regarded the pathological processes in the two cases to be different, as judged both by the naked-eye appearances and by the character of the histological changes. ZIEGLER is however quite unable to agree with him in this point: the poison of scarlatina may induce in the fauces exactly the same histological changes as those which are characteristic of diphtheria. In a still more recent and very suggestive paper (*Die experimentelle Diphtherie* Leipzig 1883) HEUBNER seems to have now arrived at a like conclusion. He indeed affirms that localized diphtheritic inflammation of a mucous membrane may be set up without micrococci, and then the inoculation of any kind of micrococci may suffice to induce the general disease.

445. **Phlegmonous inflammations** and abscesses are more common in the fauces and tonsils than in the mouth itself. They begin with intense redness and swelling of the affected parts. The exudations and pus collect in the loose meshes of the submucosa, giving rise to abscesses of various sizes, which at length break through the mucous membrane. The commonest causes of such suppurative inflammations are mechanical injury followed by some septic infection, and glanders, syphilis, anthrax, etc. Retropharyngeal abscesses are occasionally due to caries of the cervical vertebræ. Abscesses about the throat are dangerous inasmuch as they may lead to the erosion and rupture of blood-vessels, or may directly or indirectly involve the entrance to the larynx. This last accident is generally brought about by the induction of œdema in the mucosa or submucosa of the glottis, which often accompanies the formation of an abscess in the neighboring parts.

In rare cases phlegmonous inflammation may issue in gangrene. Dark and discolored patches are formed, which rapidly extend and disintegrate. Gangrene is most commonly observed in connection with small-pox, typhoid, dysentery, and diphtheria.

446. The **syphilitic affections** of the throat resemble those of the mouth. Simple catarrhal inflammation, the formation of granulomatous foci or gummata, ulceration, and scarring, are all met with. Scarring may give rise to very considerable distortion and deformity of the parts.

Tubercle and tuberculous ulceration occur chiefly in the larynx. The surrounding tissues are sometimes markedly œdematous. The tonsils are not infrequently attacked by tuberculosis.

Lupus is most apt to affect the soft palate; it is rare in other parts, such as the larynx. The infiltrated tissue breaks down and large unsightly ulcers are produced. Lupus of the face generally accompanies the affection of the mucous membrane.

Papillary growths and mucous polypi sometimes occur around the uvula and the border of the soft palate, but they are not very common. Cysts of retention, of small size, now and then arise from dilatation of the mucous glands.

Tumors are rare in the region of the throat, but both connective-tissue and epithelial growths are occasionally met with.

CHAPTER LI.

THE SALIVARY GLANDS.

447. The salivary glands are racemose glands whose secretion is discharged into the oral cavity. The chief disorders to which they are liable are those due to inflammations, and to the growth of tumors.

Mumps or epidemic parotitis is an infective inflammatory swelling of the parotid gland. The submaxillary and sublingual glands may be affected at the same time. The glands and the overlying tissues are much enlarged, and feel doughy to the touch.

Similar swellings occur as secondary symptoms in connection with certain infective disorders like typhoid, cholera, pyæmia, syphilis, diphtheria, etc.

The swelling is due to inflammatory serous and cellular infiltration of the interalveolar fibrous tissue of the glands. It issues either in resolution, or in fibroid induration, or in suppuration and abscess. Sometimes gangrene supervenes.

Angina Ludovici is an acute phlegmonous inflammation of the tissue surrounding the submaxillary gland, resulting often in suppuration or gangrene.

Milder forms of inflammation are also met with in connection with disorder of the salivary glands, resulting from mechanical injury or retention of their secretion or from other causes not easy to determine. When chronic they lead to fibrous hyperplasia, while the gland-substance often becomes atrophied. If the duct becomes involved in a contracting cicatrix it may be obstructed or altogether occluded.

448. A **salivary fistula** is an opening or channel connecting a salivary duct with the surface of the mucous membrane or the skin. It results either from a wound, or from some suppurative inflammation leading to perforation.

When a salivary duct is obstructed or occluded the smaller ducts behind the obstruction become dilated by the retained secretion. These dilated ducts are either cylindrical or sausage-shaped, or fusiform, or even pear-shaped. As the accumulation goes on the ducts and the lumen of the gland become distended into globular cysts, often of very considerable size.

The cysts produced by dilatation of the submaxillary and sublingual ducts protrude from beneath the tongue, and are often spoken of as

ranulæ, like those which arise from dilatation of the mucous glands of the tip of the tongue (Art. 439).

Salivary calculi are stony concretions which form occasionally in Stenson's and Wharton's ducts. They consist of calcium phosphate and carbonate. Sometimes they enclose foreign matters which have accidentally gained access to the ducts. According to KLEBS they also contain fungi, and these he regards as the active factors in bringing about the precipitation of the calcium salts.

Tumors both of the connective-tissue and the epithelial types are met with in the salivary glands. Of the former class fibroma, sarcoma, enchondroma, and myxoma, may be mentioned. They usually give rise to definite nodes or nodules, and sometimes include cystic cavities (cystic sarcoma). Carcinoma usually begins as an isolated nodule, which extends so as to involve the whole gland, and then invades the surrounding tissues. Ulceration and gangrene now and then supervene. These neoplasms are very apt to exhibit a mixed type of structure, especially those of the parotid gland. Thus cartilaginous, mucoid, sarcomatous, and fibroid elements may all occur within the same tumor. Sometimes the peculiar hyaline formations characteristic of cylindroma (Art. 163) are met with. Combinations of carcinoma with sarcoma or enchondroma are not uncommon.

CHAPTER LII.

THE ŒSOPHAGUS.

449. The most important of the deformities to which the œsophagus is liable is **stenosis** or narrowing of its calibre. Five varieties of stenosis have been distinguished (ZENKER, VON ZIEMSSEN) according as it is due to congenital malformation, compression, obstruction, stricture, or spasmodic contraction.

The œsophagus is wholly absent only in fœtuses which are very gravely malformed. Even a partial obliteration is rare when the fœtus is at all well-developed.

Simple **congenital** stenosis occurs both at the upper and at the lower end of the tube and may be simply annular or may extend over some small distance. Both varieties are rare.

Stenosis by **compression** is generally due to the pressure of enlarged scrofulous glands in the neck or mediastinum, mediastinal sarcoma, aortic aneurysm, etc. It produces grave functional difficulty only when the tube is in a manner encircled by the growth, so that there is no direction in which it can yield.

Stenosis by **obstruction** occurs when foreign bodies become wedged in the tube. The thrush-fungus may grow and multiply in the œsophagus to such an extent as occasionally to block up or seriously to narrow the passage. Polypous tumors growing from the mucous membrane may have a like effect, but very rarely. Cancerous growths are much more apt to be the cause of obstruction.

Strictures are due to the contraction of cicatrices or to cancerous change. Cicatrices most commonly follow upon injuries due to irritant or corrosive substances, such as boiling water, acids, or alkalies. The extent and tightness of the stricture depend on the size of the corrosion-wounds. If the corrosion has extended deeply into the tissues of the wall, the œsophagus may be transformed into a firm almost cartilaginous pipe, through which only the finest sound may be able to pass. Syphilitic strictures are very rare, as the œsophagus is on the whole seldom attacked by syphilitic inflammation. Cancerous strictures are due to the infiltration of the whole circumference of the œsophagus by the neoplasm, by which it is transformed into a kind of tough unyielding tube, the infiltrated tissue often at the same time undergoing contraction. These strictures are usually found in the lower or middle third of

the œsophagus, rarely in the upper third; they extend over a length of 5 to 10 centimetres. The inner surface is in general ulcerated.

Spasmodic or spastic stenosis is due to a painful contraction of the muscular coats. It is transient but apt to recur, especially in hysterical patients. As a rule no appreciable anatomical lesion of the œsophagus can be made out *post mortem;* though sometimes inflammation or ulceration of the mucous membrane exists and may induce abnormal irritability and spasm.

The channel may, on the other hand, be abnormally wide, either from dilatation or from the presence of diverticula.

Simple **dilatation** is generally the result of stenosis of the lower part of the tube or of the cardiac orifice of the stomach. In this case the muscular walls yield and become distended as the ingested food gathers above the contracted portion. The dilatation is generally uniform, but occasionally it is unilateral and in this way diverticula are sometimes produced. The various coats are often thickened in the dilated portion.

But dilatation may take place without stenosis; and in this case the œsophagus assumes the form of a fusiform sac, the walls of which (and especially the muscular and epithelial coats) are more or less thickened. The apparent cause of the dilatation is a diminution of the contractile power of the walls, due to injuries of various kinds or to inflammatory change. Localized dilatations above the diaphragm occur as congenital malformations (ZENKER).

Diverticula occur as localized sacculations at some part of the wall of the pharynx or œsophagus. They are due to pressure from within, or traction from without.

Diverticula of the former class are rare. They occur at the lower end of the pharynx, and appear either as small sacculations of the size of a hazel-nut or less and directed posteriorly, or as large globular, cylindrical, or pyriform sacs hanging down between the tube and the spine. The walls of such a sac are moderately thick and consist of the mucosa and submucosa with an external adventitious layer of fibrous tissue; the muscular coat is absent or persists only around the neck of the sac. The diverticulum is in fact a hernia (pharyngocele) of the mucous membrane through the muscular bundles of the inferior constrictor of the pharynx. ZENKER accounts for its existence by supposing that some localized weakening of the posterior wall of the pharynx takes place, and that then the inner layers are pushed through the outer by pressure from within exerted in the act of swallowing. The weakening may be due to mechanical injury, such as that caused by the lodgment of a foreign body. As food sometimes lodges in a diverticulum and remains there decomposing for a time, it may act as an irritant to the mucous membrane and give rise to inflammatory thickening of the wall, or occasionally to mucous papillary growths from its inner surface.

Diverticula due to traction occur on the anterior aspect of the œsophagus, and most commonly at the level of the bifurcation of the trachea. They are usually narrow and funnel-shaped, varying in depth from 2 to 17 mm., the apex pointing directly forwards or a little to one side. Simple shallow bulgings are more rare. The funnel consists of mucosa and submucosa, which may be wholly or partially or not at all covered with a muscular layer. The apex almost invariably runs out into a band of dense fibrous tissue, generally containing a shrunken bronchial gland and connected with the trachea or one of the bronchi. The diverticulum thus appears to be ultimately due to an inflammatory process starting in some lymphatic gland and involving the wall of the œsophagus: the contraction of the inflammatory or cicatricial tissue gives rise to the traction upon the œsophagus-wall. The diverticulum has no tendency to enlarge, but it may be perforated by a foreign body which becomes wedged in it.

Rupture of the healthy œsophagus is rare, if we leave out of account the cases in which it is directly wounded from without. There are however some instances on record in which strangulation or violent vomiting have led to longitudinal or transverse rents of the wall. It may be that in the latter cases the tissues were to some extent softened by the action of the regurgitated gastric juice. This digestive softening is not uncommon as a post-mortem phenomenon: the affected tissue appears gray or yellow and sodden, and is readily torn. According to ZENKER it may occur *in articulo mortis;* but the instances must be very rare in which it occurs in a healthy patient.

Perfora ion of the œsophagus is due to disease in the tube itself or in the adjoining parts. Cancerous ulceration and the lodgment of foreign bodies are the commonest causes of the former; corrosion by various liquids and simple ulceration come next in point of frequency. Perforation from without may be due to suppurating lymphatic glands, abscesses, gangrene of a goitrous tumor, or aneurysm of the transverse or descending aorta. Perforation is always followed by more or less extensive inflammation. This is least marked when the tissue around the ruptured spot is already thickened by chronic inflammation. When there is no such thickening, widespread purulent or gangrenous inflammation may be set up in the neighboring parts.

ZENKER and VON ZIEMSSEN (*Ziemssen's Cyclopædia* VIII.) give a very minute and accurate account (with full references to the literature) of the morbid changes to which the œsophagus is liable. The above account is based upon theirs.

450. **Catarrhal inflammation** of the œsophagus is marked chiefly by epithelial desquamation; but little mucus is poured out in the chronic forms, and in the acute forms it is absent. The desquamated cells give the mucous surface a dull whitish or yellowish tint. Sometimes minute superficial ulcerations occur. When the inflammation is caused

by the presence of a foreign body, a deep ulcer is often formed at the spot where it is in contact with the wall.

In chronic catarrh the mucous membrane may become hypertrophied, and papillary or polypous outgrowths are apt to arise from its surface: the muscular coat may also show signs of hypertrophy. If the mucous glands become obstructed they give rise to granular prominences which are liable to break down and leave minute ulcers. Varicose veins are not infrequently met with in the œsophagus in elderly patients. They lie in the submucosa, and give rise to small livid prominences of the mucous membrane. When these become eroded minute ulcers exactly resembling the ulcers of chronic catarrh are formed, and are described as varicose ulcers. Serious hæmorrhage sometimes occurs when a varicose vein gives way.

Croupous and **diphtheritic inflammations** are rare. They occur most frequently in connection with typhoid, cholera, measles, scarlatina, small-pox, pulmonary tuberculosis, and pyæmia: they very seldom indeed accompany ordinary diphtheria. Sometimes in the course of small-pox regular variolous pustules appear in the œsophagus.

Phlegmonous inflammation occurs either localized or diffused over a considerable area: it is however an extremely rare affection. If the collection of pus which forms in the submucous tissue breaks through the surface, complete repair and recovery may ensue. When the phlegmonous abscess is larger, undermining a considerable portion of the mucous layer and breaking through it at several points, some part of the cavity of the abscess may persist unhealed after its evacuation: it becomes gradually covered over with epithelium growing in from the sites of perforation. This variety of inflammation is due to wounds or corrosions, or to the extension upwards of a phlegmonous inflammation of the stomach, or to purulent inflammation extending inwards from the surrounding tissues.

Corrosive substances like sulphuric, nitric, hydrochloric, or carbolic acids, caustic potash or soda, blue vitriol, etc., give rise to more or less wide-spread destruction of the œsophageal tissues. If the acids are dilute the epithelium alone may be destroyed, becoming white and turbid and falling away from the mucosa. If the corrosive action goes further, the mucous membrane in its whole thickness is transformed into a gray or brown or black slough traversed by blackened blood-vessels, and sometimes the muscular coat is destroyed likewise. If the patient survives violent inflammation results, which is usually suppurative and now and then leads to perforation. When however the suppuration causes the necrosed tissue to separate, the wound may become scarred over; if the muscular coat has been destroyed the scar invariably contracts and gives rise to extreme constriction of the tube.

Patients who are much emaciated and bedridden sometimes suffer from gangrenous ulceration of the pharynx. Gray or black sloughs form

on the anterior and posterior wall at the level of the cricoid cartilage, which are presently cast off leaving ulcers behind them. The affection is due to the continuous compression of the tube between the larynx and the spine, the extreme relaxation of the muscles permitting the larynx to sink down on the yielding pharynx. It is therefore of the nature of a bed-sore or **decubital necrosis** (Art. 33).

Syphilitic inflammation and ulceration of the œsophagus are extremely rare.

* 451. **Connective-tissue growths** are not common in this region, though fibroma, lipoma, myxoma, and sarcoma are sometimes met with. As a rule they form globular polypous-looking tumors. This is especially true of fibroma, which occasionally develops in the lower part of the pharynx behind the larynx and hangs pendulous within the tube.

Papillary outgrowths from the mucous membrane are more common; they somewhat resemble warts in general structure.

Carcinoma is however by far the most important of the neoplasms affecting the œsophagus. It may appear at any point of the tube, though it is most frequently met with in the lower third. It gives rise to isolated or annular infiltrations, which speedily break down into ulcers. Sometimes the protuberant parts of the growth are entirely removed by ulceration, while the base and margins of the sore continue to be infiltrated with cancer-tissue. The disease extends in the first instance to the muscular coat, and then to the adjacent tissues and organs. The connective tissue surrounding the œsophagus becomes indurated and beset with nests of cancer-cells; then the trachea, bronchi, pericardium, heart, pleura, lungs, etc., may be successively invaded. Perforation may result from the ulceration, and then ulcerative disintegration spreads rapidly through the previously infiltrated organs. The neighboring parts are always more or less inflamed. Primary cancer of the œsophagus is a squamous epithelial carcinoma (Art. 173).

With regard to **thrush** see Arts. 436 and 449.

CHAPTER LIII.

THE STOMACH.

452. **Introductory.** With the **stomach** begins the portion of the alimentary tract whose special function is the digestion and absorption of the ingested food. In acordance with this function we find the mucous membrane of the stomach furnished with numerous blood-vessels and lymphatics, a very thin epithelial covering, and an extraordinary number of glands yielding the juices necessary for digestion.

The ingesta linger in the stomach for a considerable time; part is directly absorbed by the gastric mucous membrane, part is altered by the gastric digestion, and part passes on unaltered.

It is easy to understand that—owing to the length of time during which the ingesta remain in the stomach, and the intimate nature of the relations between them and the mucous membrane—the latter is very liable to be injuriously affected by any noxious substance which may be swallowed. Thus the acids and alkalies which give rise to swelling and corrosion in the mouth, throat, and œsophagus (Art. 450) will in general act still more destructively on the walls of the stomach. And other substances (like phosphorus, salicylic acid, etc.), which may pass through the upper parts of the tract without doing any harm, will be able in the stomach, where they lie for an appreciable time, to set up local or general inflammatory mischief. An excessive meal of ordinary food may have the latter effect, and of course substances in themselves noxious or irritating will act more intensely. And although the stomach has the power of as it were protecting itself by the secretion of a thick coating of inert mucus, still this power has its limits and often enough is inadequate.

The gastric mucous membrane is likewise exposed to danger from the side of the circulation. Apart from local or general disturbances of the blood-supply leading to anæmic necrosis and hæmorrhage, to abnormal secretion, or to œdema, we may have noxious matters conveyed by the blood to the membrane, and setting up in it degenerative changes of various kinds. Thus cloudy swelling and fatty degeneration (Arts. 48, 50) of the gland-cells are met with in connection with many infective and toxic affections, such as small-pox, typhoid, septicæmia, and phosphorus-poisoning. Often the degeneration is so marked as to give rise to obvious macroscopic change, the mucous surface taking on a turbid grayish or yellowish tint. The stomach suffers also in connection with other

general diseases. Thus in cases of generalized amyloid disease the fibrous structures of the gastric blood-vessels are often affected by amyloid degeneration.

453. Morbid changes in the walls of the stomach involve more or less grave disturbance of its digestive functions. This disturbance again may set up others, and these may give rise to further morbid changes of a secondary kind.

The gastric secretion in health is such as to induce in the ingested food certain definite chemical changes. If the secretion is from any cause deficient or morbidly altered, the ingesta may undergo abnormal decompositions. These are very often of the nature of fermentations set up by fungi of various kinds. These fungi or their germs are swallowed with the food; but in health they do not develop or multiply within the stomach, the gastric secretion being unfavorable to their growth. When however this property of the secretion is altered or inactive, the fungi are free to flourish.

Over-distention of the stomach and stagnation of its contents favor the growth of fungi in it. Permanent dilatation may be induced by too frequent or too abundant meals; but it is more commonly due to some obstruction or to atony of the muscular coat. These again may depend on very various causes. In the first place the free passage onwards of the food may be interfered with by such causes as habitual stooping, tight-lacing, the pressure of abdominal tumors, etc. The same effect is produced, but in a much higher degree, by textural changes in the stomach itself—especially by stenosis of the pylorus, inflammatory infiltration and induration of the walls, gastric ulcers and cancers, adhesions to contiguous organs, degeneration and other affections of the muscular coat, etc. And when from any cause the digestive function is disordered, the onward movement of the food may be hindered by the pyloric sphincter refusing to relax, the usual stimulus of the normally-digested chyme being absent (Brücke, *Physiologie* I.).

When any of these conditions give rise to considerable accumulation of undigested food in the stomach, the fungi grow and multiply, sometimes to an enormous extent. Micrococci, microbacteria, bacilli of the most various forms, sarcinæ, yeast-fungi, all flourish luxuriantly. In the contents of an atonic and chronically dilated stomach we may often find specimens of almost every type of these organisms. Sometimes we may also meet with spores of filamentous fungi or moulds, such as *Mucor*.

In consequence of the growth of these fungi fermentations of various kinds are set up. The chief of these are the lactic, butyric, acetic, alcoholic, and certain varieties of septic or putrefactive fermentations.

These abnormal fermentations naturally react injuriously on the stomach and on its power of secretion. They keep up an abiding irritation of its mucous membrane, and often seriously hinder the repair of

the original lesion, which may be in itself but slight and transient. In some cases the bacteria attack the mucous membrane directly. Thus according to VON RECKLINGHAUSEN (*Virch. Arch.* vol. 30) and VON WAHL (*Virch. Arch.* vol. 41) certain kinds may penetrate the glands and the underlying tissue, and give rise to pustule-like nodules protruding above the surface. In the case of a man who died after two days' illness with choleraic symptoms, the author found the stomach beset with small whitish patches of necrosis and minute ulcers with whitish floors; and on examination these were seen to contain multitudes of bacilli. Mould-fungi and yeast-fungi are unable to penetrate the mucous membrane.

When the contents of the stomach are highly acid while the circulation within its walls is somehow weakened, the walls may become softened or macerated, or in a certain sense digested. According to the amount of blood it contains the mucous membrane is transformed into a brown or black pulpy or jelly-like friable mass. This 'softening of the stomach' (**gastromalacia**) is generally met with in cases of brain disease, especially in tuberculous meningitis where it may set in during the last hours of life. LEUBE is of opinion that it may occur in persons previously in good health, but his instances are by no means conclusive.

Gastromalacia is in the great majority of cases a post-mortem phenomenon. After death the mucous membrane of the stomach alters very quickly, especially when it contains an excess of gastric juice or of acid products of decomposition.

The first alteration consists in solution of the blood-corpuscles and diffusion of their coloring-matter through the tissues. If sulphuretted hydrogen is evolved from the contents of the stomach, the red coloring-matter is changed to greenish-black. Brown pigmentations, such as occur in cases of chronic gastritis, take on a gray or black tint.

Self-digestion very frequently follows. The mucous membrane and then the muscular and serous coats are transformed into a soft friable mass, white or gray or black in color. When the stomach is lifted out its contents sometimes break through the softened tissue and escape. Occasionally the walls are thus macerated over their entire extent; and when the fundus has been lying in contact with the diaphragm, the process may extend to the latter and so break it down that the contents of the stomach escape into the thorax. The most marked instances of self-digestion of the stomach occur in young children, whose stomachs contain a large quantity of undigested milk; and the characteristic appearances are more frequently seen in hot weather than in cold.

References on mechanical dilatation and fermentation within the stomach:—KUSSMAUL, *Deut. Arch. f. klin. Med.* VI.; JÜRGENSEN, *ibid.* VII.; PENZOLDT, *Die Magenerweiterung* Erlangen 1875 (with full references); LEUBE, *Ziemssen's Cyclop.* VII, *Deut. Arch. f. klin. Med.* XXIII.; NAUNYN, *ibid.* XXXI.; POENSGEN, *Die motor. Verrichtungen d. menschlichen Magens* Strasburg 1882; BUDD, *Organic diseases of the stomach* London 1855; FENWICK, *The stomach and duodenum* London 1868; EWALD, *Die Lehre von d. Verdauung* Berlin 1879; ROSENBACH, *Samml. klin. Vorträge* no. 153.

On gastromalacia see ELSASSER, *Die Magenerweichung der Säuglinge* Stuttgart 1846; LEUBE, *Ziemssen's Cyclop.* VII.; KUNDRAT and WIEDERHÖFER, *Ger-*

hardt's Handb. d. Kinderkrankh. IV.; THORSPECKEN, *Deut. Arch. f. klin. Med.* XXIII.; W. MAYER, *Gastromalacia ante mortem*, *ibid.* IX., In. Diss. Leipzig 1871.

454. **Congenital anomalies.** The stomach is occasionally absent in acephalic monsters. More rarely it is found to be abnormally small, in fœtuses which are otherwise well-developed. Complete atresia of the pylorus is very rare, but stenosis or abnormal contraction is more frequent (R. MAIER).

Of congenital anomalies of form we may mention abnormal constrictions of the body of the stomach, giving it an hour-glass shape; and the occurrence of partitions abnormally subdividing it.

In cases of *Situs tranversus* or lateral transposition of the viscera (Art. 11), in persistent fissure of the abdomen and thorax (Art. 9), and in congenital deficiency of the diaphragm, the stomach is as a rule misplaced. Sometimes the vertical position of fœtal life persists in the adult.

Acquired anomalies of form and position are more common. Dilatation may be due to congenital or acquired stenosis of the pylorus. But it may occur independently of pyloric obstruction, as a result of abnormal position or adhesions, of distention from excess of ingesta, or from textural changes in the walls (Art. 453).

In extreme dilatation the stomach occupies a large extent of the abdominal cavity, extending backwards rather than forwards. It may reach from the left side of the diaphragm to the symphysis pubis, compressing the bladder and covering over almost the whole of the intestinal convolutions. The left half of the lesser curvature runs parallel to the spine, in continuation of the line of the œsophagus: the pyloric half bends up at a sharp angle towards the liver. The greater curvature lies along the left side of the abdomen, the pylorus being dragged downwards and backwards and the hepatico-duodenal ligament stretched. The coats of the stomach may be thinned in every part or, according to the cause of the dilatation, may be thickened at various spots, especially in the neighborhood of the pyloric end.

Acquired contraction or constriction of the stomach is due either to functional inactivity of the organ as in prolonged starvation, or to inflammatory or ulcerative disease leading to cicatricial contraction. Peritonitis, followed by adhesions and contraction of the serous membrane (*peritonitis deformans*), may give rise to shrinking or other deformity of the stomach. Partial alterations of form are due to local disease. Ulcers (chiefly along the lesser curvature) which heal and become cicatrized lead to retractions and constrictions, which may be so extreme as to give the stomach the form of an hour-glass, or to bring the cardiac and pyloric ends into contact. New growths in the stomach-wall may have like effects. Gastric diverticula are very rare.

Displacements of the stomach as a whole may be caused either by changes in the surrounding parts or by disorders of the organ itself.

References:—PENZOLDT, *Die Magenerweiterung* Erlangen 1875; LANDERER, *Die angeborene Stenose des Pylorus* Tübingen 1879; DEMME, *Die Magenerweiterung beim Kinde, Jahresbericht d. Kinderspitales* Berne 1882.

455. **Hypertrophy** of the muscular coat is observed in like conditions to those which are associated with dilatation, namely in cases of pyloric obstruction. It is rarely met with unaccompanied by such obvious anatomical lesions as explain its development; when these are absent we are driven to refer it to functional disturbance of some kind (NAUWERCK, *Deutsches Archiv f. klin. Med.* XXI.). The hypertrophy is most marked near the pylorus, less so about the fundus; it may be very considerable.

Notable thickening of the walls of the stomach may follow upon chronic inflammation (Art. 456), and is common in carcinomatous disease (Art. 461). In both cases the thickening is mainly due to fibrous hyperplasia, though the mucous and serous coats and at times the muscular coat partake in the change: cases are however not rare in which the muscular coat is decidedly hypertrophied. The fibrous thickening which accompanies carcinomatous disease is often very great.

Gastric polypi are papillary outgrowths from the mucous membrane of an inflammatory kind (Art. 456). They vary from the size of a pea to that of a hazel-nut or more, and very frequently enclose small cyst-like cavities. No new glands are formed in them, although by the overgrowth of the interglandular tissue single glands here and there may seem enlarged. Such inflammatory polypi are to be distinguished from the villous or papillomatous neoplastic growths or true tumors which may occur in the stomach.

Atrophy of the coats is met with in conditions of general cachexia, and in cases of dilatation. Fatty degeneration of the muscular fibres takes place, and according to R. MAIER colloid degeneration also occurs. When the fibrous elements become hyperplastic the muscle-cells may be compressed and undergo atrophy, while the glandular structures also dwindle and degenerate (Art. 456).

456. **Inflammation of the stomach** or **gastritis**. In recent acute catarrh (acute gastritis) the mucous membrane of the stomach appears dark-red and swollen, and beset with small hæmorrhagic patches. The surface is covered with a film consisting of mucus, mucoid epithelium, and extravasated leucocytes. The cylindrical epithelial cells of the gland-ducts, which in normal conditions manufacture large quantities of mucus from their protoplasm, are seen to have passed into an extreme stage of mucoid change, and many are in process of desquamation. The epithelial cells of the peptic glands lie loosely in the lumen, and seem more granular than usual. The vessels of the interglandular connective tissue are distended, and their course is marked by cellular infiltration of the tissue, especially along the small veins. The subglandular tissue, and in some cases the submucosa, are here and there infiltrated; the endothelium of the lymphatics is swollen and desquamating, and some

of the cells are multinuclear. These signs of inflammation may appear over the whole extent of the mucous membrane, or may be confined to a few patches; very often the pyloric end alone is affected. Acute catarrhal gastritis is in most cases a transient affection, resulting in resolution and recovery; but it may pass into the chronic form and so lead to permanent changes.

Thus the infiltration and the epithelial desquamation may become extreme; part of the epithelium is thus permanently lost, and as the desquamation extends the glandular structures gradually perish. In other words, atrophy of the mucous membrane takes place. In rare cases this is accompanied by disintegration of the fibrous sub-structures. Where the infiltration has been greatest, perhaps where hæmorrhagic extravasation has occurred, both epithelium and fibrous tissue perish, and are cast off in larger or smaller fragments (see Art. 421). In this way more or less extensive **ulceration** is set up, and may spread over a large part of the mucous membrane.

The individual ulcers are of various sizes. The floor is usually irregular and beset with low ridges or with small warty elevations; they may be pale or red, and are sometimes indurated. The margins pass gradually into the thinned and atrophied membrane around, or are sharply defined and marked by the presence of excrescences in the form of small polypi or raised borders. Whenever the ulcer is large enough to be easily visible, the glandular structures of the mucosa are found to be almost wholly destroyed. The muscularis mucosæ usually persists, but is thickly beset with infiltrated cells. The submucosa is thickened, indurated, and infiltrated, its fibrous elements being hyperplastic and abnormally coarse in texture. The glandular structures, where they remain, are infiltrated with leucocytes; the infiltration being most marked in the neighborhood of the thickenings and polypous excrescences. Some of the glands undergo cystic degeneration. The lymphadenoid follicles are fuller of lymphoid cells than in normal conditions, and are somewhat enlarged.

Ulcers of this extent are rare as a consequence of simple inflammation. Like the round or perforating gastric ulcer (Art. 459) they may give rise to serious hæmorrhage.

A more common result is pigmentary change in the mucous membrane, with glandular atrophy and fibrous hyperplasia (**atrophic pigmentary induration**). The pigmentation is usually gray, and is due to the presence of minute black granules derived from small extravasations of blood. The atrophy appears in the thinning of the mucous membrane, which may be marked enough to be visible by the unaided eye; in slighter cases it can be demonstrated under the microscope.

When the fibrous hyperplasia is on the whole but slight, it seems to be confined to the interglandular connective tissue (Fig. 175 *a*). In more advanced cases the mucous membrane is increased in its entire

thickness, and rises in folds (*d*) and warty or polypous excrescences. The surface thus becomes rough and corrugated, and the condition is known as the *état mamelonné*, or *polyposis ventriculi* (Art. 422).

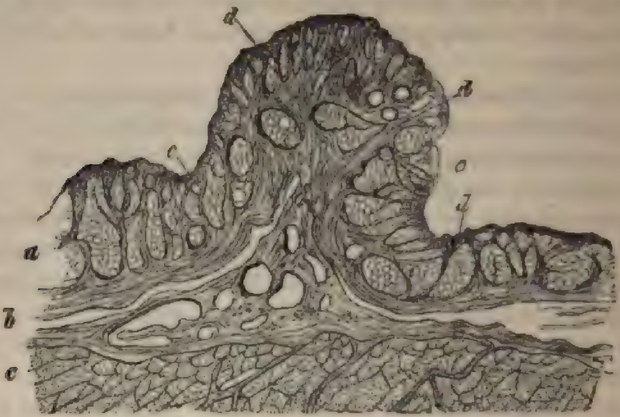


FIG. 175. FIBROID FOLD (*ETAT MAMELONNE*) IN THE GASTRIC MUCOUS MEMBRANE.

(*Hæmatoxylin staining*. × 10.

a, mucosa, with atrophied glands.
b, submucosa.
c, muscular coat.
d, hyperplastic fibrous tissue of the mucosa.
e, gastric glands.

The hyperplastic fibrous tissue (*d*) may be dense and coarse-fibred, or soft and cellular. Some of the glands lose their epithelium and disappear, others take the form of cysts. These cysts, which vary in size from that of a small pea to that of a bean, contain a clear viscid liquid mingled with granular detritus and sometimes transparent spherules of colloid substance. The epithelium of the cysts is cylindrical (Fig. 176 *c*), and many of the cells have the appearance of typical goblet-cells. The larger cysts are occasionally beset with papillary ingrowths from their walls (Fig. 176 *c*).

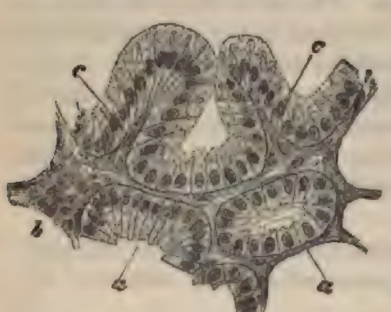


FIG. 176. SECTION THROUGH A GASTRIC POLYPUS.

(*Hæmatoxylin staining:* × 300.)

a, tubular gland with cylindrical epithelium.
b, fibrous stroma infiltrated with leucocytes.
c, papillary growths into the lumen of a glandular cyst.

In all forms of chronic inflammation, but especially in the ulcerative forms, the overgrowth of fibrous tissue may extend to the submucous, muscular, and even to the serous coats.

The wall of the stomach is thus thickened and indurated, while the muscular fibres are more or less compressed and atrophied. In other instances, however, the muscular coat becomes hypertrophied.

457. **Phlegmonous inflammation** of the stomach is rare; it may be general or circumscribed, the latter being the commoner form. The seat of the inflammation is essentially the submucosa (compare Arts. 390, 427).

In the circumscribed form, more or less extensive **abscesses** may be formed and break into the cavity of the stomach. In the diffuse form the submucosa is at first greatly swollen and thickened, while the mucosa is unaffected or occasionally somewhat swollen. The exudation in the submucosa is sero-purulent, and the mucosa is infiltrated with round-cells. Sometimes the infiltration extends to the muscular coat, passing chiefly along the intermuscular septa. In this way the serous coat may come to be affected in like manner. Both muscular and serous coats then become swollen, and the serous surface may be covered with purulent or fibrino-purulent deposits.

After a time the submucous tissue appears to break up and dissolve, and the exuded pus breaks at various points through the mucosa. The latter becomes in some cases almost riddled such perforations. The muscular coat may likewise suppurate. If the patient survive, the smaller openings may cicatrize over and so heal, but the larger frequently remain as cavities extending into the submucosa and ultimately become covered internally with a stratum of epithelial cells; such cavities may communicate with the cavity of the stomach by one or more openings through the mucosa.

Croupous and **diphtheritic inflammations** of the gastric mucous membrane are rare. They are generally met with in connection with diphtheritic pharyngitis in cases of scarlatina or small-pox, and in infants who die of septic inflammation of the umbilicus.

The croupous exudation takes the form of more or less extensive grayish-yellow false membranes; but these very rarely extend over any large part of the gastric surface. In diphtheritic inflammation the necrotic membrane may consist only of the superficial epithelial cells (and then appears as a small grayish patch); or it may include the whole thickness of the mucosa, which is then transformed into a gray or black slough. Ulcerations due to small-pox, tuberculosis, typhoid, or syphilis, are very rarely met with in the stomach.

Corrosion of the stomach by caustic poisons is comparatively common. It is always associated with like changes in other parts of the alimentary canal above and below the stomach. In the latter case the changes may extend to the ileo-cæcal valve, owing to the fact that the small intestine is much more easily affected by such poisons, even when much diluted, than the stomach.

All corrosive poisons, whether acids or alkalies, when concentrated give rise to sloughing and separation of the superficial layers of the mucous membrane (A. Lesser). The sloughs or eschars caused by sulphuric acid are grayish-white or ashy-gray, dry and coarse in appearance, and

brittle. In extreme cases the entire surface may be transformed into a charred-looking blackened mass. When recent the several elements of the tissue are still recognizable in the slough, though they are turbid and shrunken. The sloughs due to hydrochloric acid are similar. Nitric acid produces a yellow or orange slough. The color of the less affected parts is pale purple or grayish. Oxalic acid gives rise to slight and superficial sloughs, which are white or grayish in color. A concentrated solution of caustic potash acts like sulphuric acid, but the sloughs are less brittle. Parts that have been for some time in contact with the alkali become semi-transparent. Corrosive sublimate, carbolic acid, and arsenious acid, give rise to white sloughs.

The mineral acids and alkalies are the most powerfully corrosive. Not only may all the coats of the stomach be destroyed by their action, but the neighboring organs may be similarly corroded and discolored. The liver and spleen are especially liable to be attacked, and then look almost as if they had been boiled.

In the parts surrounding the sloughs, and in other places where the poison has been somewhat diluted, a more or less intense hæmorrhagic inflammation is set up. The parts thus affected presently take on a brownish, greenish, or grayish-black tint, and are traversed by blackened vessels; the slough at the same time softens or breaks down, and this more readily in the case of acids than of alkalies. By and by the dead tissue is cast off and liquefies.

The most intense inflammation is that set up by the strong mineral acids; oxalic acid, corrosive sublimate, carbolic acid, and arsenious acid, are much less active in this respect.

If the patient does not straightway die, the corrosion-wounds may heal by cicatrization. Where the corrosion has been extensive, very great contraction and deformity of the stomach and intestine may result.

References on corrosion of the alimentary tract:—CASPAR and LIMAN, *Handb. d. gerichtlichen Medicin* Berlin 1881; BÖHM, *Ziemssen's Cyclop* XVII.; BIRCH-HIRSCHFELD, *Lehrb. d. path. Anat.* 1877; VIRCHOW, *Charité-Annalen* VI., 1881; A. LESSER, *Virch. Arch.* vol. 83; FILEHNE, *ibid.* vol. 83; TAYLOR, *Medical Jurisprudence* London 1883.

458. The gastric mucous membrane is very liable to **hæmorrhage.** Hæmorrhage may be caused by traumatic injury through the swallowing of solid bodies or corrosive poisons, by inflammatory changes in the blood-vessels, by ulceration, by venous engorgement such as accompanies portal obstruction in various hepatic disorders, scurvy, yellow fever, acute yellow atrophy of the liver, typhoid, etc.; in fact by local lesions and by general infective disease, by constitutional disorder and by changes in the composition of the blood as a whole. In rare cases hæmorrhage may be due to primary alterations, such as atheroma and aneurysm, in the large vessels of the stomach and the neighboring organs.

The effused blood, which may be small or large in quantity, becomes rapidly brown or black as the gastric acids transform its hæmoglobin into hæmatin.

When the bleeding is due to the erosion or rupture of a small blood-essel, the fact can in general be easily verified on opening the stomach. When the bleeding is 'capillary' or parenchymatous the tissue is infiltrated with blood and red, brown, or black in color. Such infiltrated tissue is of course more or less completely deprived of circulating blood, and is consequently exposed to the digestive action of the gastric juice. It is therefore attacked and in part dissolved, and in this way an ulcer or 'hæmorrhagic erosion' is produced.

Hæmorrhagic erosions of the stomach heal in the same way as those of other mucous membranes, unless some special obstacle stands in the way. If the loss of substance is at all considerable a reactive inflammation is set up, in consequence of which the surrounding parts become infiltrated with cells. Granulation-tissue and a cicatrix are produced, and presently become clothed with epithelium. The same process takes place in the healing of other lesions unaccompanied by notable hæmorrhages, such as those caused by traumatic injury, corrosive poisons, etc.

The result is different in certain conditions unfavorable for repair, as when the gastric acids are present in excessive quantity, or when the circulation in the parts around the erosion is interfered with for any reason, local or general (*e.g.* anæmia). In such cases the circulation in the floor and margins of the erosion may be insufficient to protect the parts from digestion. The exposed strata of the tissue are dissolved one after another, and an ever-enlarging ulcer is produced, the so-called *ulcus ex digestione* (Art. 459). When thrombosis occurs in the vessels exposed by an erosion such an ulcer is very apt to be produced.

Melæna neonatorum is a peculiar form of hæmorrhage from engorgement. It is a gastro-enterorrhagia, or bleeding from stomach and intestine simultaneously, which appears in the first week or two of life, most commonly in the first to the third day. It occurs in strong healthy infants as well as in those who are born semi-asphyxiated; and is probably due to some disorder or defect of the circulation after birth, such as often leads to temporary engorgement or congestion. If the mucous membrane be thus at any point infiltrated with blood, an ulcer may afterwards be readily formed. The stomach and duodenum are the commonest seats. According to LANDAU the arteries of the stomach and intestine are liable to embolism from fragments of thrombi forming in the umbilical vein and ductus arteriosus; and the embolism may give rise to hæmorrhagic infarction, hæmorrhage, and ulceration. See BUHL (*Klinik f. Geburtskunde* 1864), SPIEGELBERG (*Jahrb. f. Kinderheilk.* II. (new series) 1869), LANDAU (*Ueber Melæna d. Neugebor.* Breslau 1874), REHN (*Centralzeitung f. Kinderh.* I.); WIEDERHÖFER *Gerhardt's Handb. f. Kinderkr.* IV.).

459. **Round or perforating gastric ulcer** (*ulcus rotundum, ulcus perforans, ulcus simplex*, or *ulcus ex digestione*). 'Round' ulcer occurs in the stomach or duodenum, and very rarely in the lower part of the

œsophagus. As we have said in Art. 458, it is due to the digestive action of the gastric juice, and takes the form of a circumscribed progressive necrosis with solution of the necrosed tissue.

A typical perforating ulcer measures from one to six centimetres across, and in form resembles a flat funnel or saucer, inasmuch as the loss of substance in the mucosa or surface layer is greater than that in the other layers. Where the submucosa rests on the muscular coat a slight ledge or terrace can generally be made out. In ulcers that are not recent these relations often disappear, the loss of substance in the deeper layers (muscular and serous) becoming as great as in the more superficial ones. Such ulcers may be as much as eight to twelve centimetres in diameter.

When the ulcer extends through all the coats, as it not infrequently does, the adjacent organs, like the pancreas and liver, are usually found to be bound to the stomach by firm adhesions and so come at length to constitute the floor of the ulcer. In such cases the cavity may become flask-shaped, the hole in the stomach-wall leading into a larger excavation in or bounded by the underlying viscera.

The margins of the ulcer are usually smooth, and not thickened; at most they are slightly swollen. On microscopic examination it appears that no appreciable amount of cellular infiltration precedes or accompanies the disintegration of the tissue. The inflammatory processes which give rise to the adhesions between the stomach and the adjacent organs, and to the thickening of the serous coat, are secondary to the progressive destruction by the gastric juice.

Any kind of injury which causes a localized textural lesion of the mucous surface of the stomach, and so expose it to the unchecked action of the gastric juice, may be the originating cause of a gastric ulcer. Probably the commonest of such causes are venous engorgement, hæmorrhage, and arterial anæmia (ischæmia) due to embolism, spasmodic contraction, or sclerosis. In other cases mechanical injury, or corrosion by caustic substances, may afford a starting-point. AUFRECHT has succeeded in producing typical gastric ulcers in rabbits by injecting cantharidin under the skin (*Cent. f. d. med. Wiss.* 31, 1882). He regards these ulcers as depending primarily on an intense hæmorrhagic inflammation of single gastric glands (gastradenitis).

Gastric ulcer runs a chronic course, but the first stages of its development are often somewhat rapid. After severe burns of the skin, for example, ulcers of the stomach and duodenum are sometimes very rapidly induced, probably in consequence of some vascular obstruction or thrombosis due to disintegrated blood-corpuscles (Art. 262). Round ulcers are most frequently met with in the neighborhood of the lesser curvature, then near the pylorus, and least frequently in the duodenum.

Dangers in gastric ulcer. When an ulcer has once formed it may heal up, provided it is not too large. For this it is necessary that a good

circulation should be established in the structures of the floor and margins; the tissue thus becomes alkalized and fortified against the action of the gastric juice, and the formation of granulations and cicatricial tissue becomes possible.

Small ulcers may heal without leaving any marked scar. Ulcers of any size give rise to dense puckered scars, which by their **contraction** may cause considerable deformity of the stomach. An ulcer near the pylorus may lead to dangerous stricture of the orifice.

One great danger in gastric ulcer arises from the risk of **hæmorrhage** from small or large arteries, which become eroded in the course of the ulcerative process. The hæmorrhage may recur again and again and lead to extreme anæmia, or a single great hæmorrhage may bring about death directly. On post-mortem examination it is not rare to find in the floor of the ulcer the eroded vessels, either patent or closed by thrombi, from which the bleeding has taken place. Occasionally one of the larger vessels, such as a main branch of the coronary or splenic artery, is found to have given way.

A still greater danger is that of **perforation** into the peritoneal cavity. This may happen whether adhesions have been set up between the stomach and neighboring organs, or not. In the former case the adhesions are torn asunder and the contents of the stomach escape. Fatal peritonitis is the usual result.

The organs which adhere to the floor of the ulcer, such as the pancreas or liver, usually exhibit fibrous thickening and hyperplasia at the surface of adhesion. Notwithstanding this the contents of the stomach may break through into the substance of the organs, and give rise to abscesses in their parenchyma. Sometimes adhesions occur between the stomach and the duodenum or transverse colon. When perforation takes place in such a case a fistulous communication may be opened between the intestine and the stomach. In like manner rupture into the pleural or pericardial sac may occur, and in the latter case may lead to erosion and perforation of the heart-wall itself (BRENNER, *Wien. med. Woch.* 48, 1881).

References on simple gastric ulcer (*ulcus rotundum*):—VIRCHOW, *Virch. Arch.* vol. 5; KLEBS, *Handb. d. path. Anat.* I.; BUDD, *Organic diseases of the stomach* London 1855; BRINTON, *Ulcer of the stomach* London 1857, *Diseases of the stomach* London 1864; FENWICK, *The stomach and duodenum* London 1868; VON ZIEMSSEN, *Sammlung klin. Vorträge* no. 15; GERHARDT, *Wiener med. Presse* 1867; GÜNSBURG, *Arch. f. physiol. Heilk.* XI.; KEY, *Hygeia* 1870; WILSON FOX, *The diseases of the stomach* London 1872, with reference to English papers; PANUM, *Virch. Arch.* vol. 25; COHNHEIM, *Allg. Path.* II. Berlin 1882; KÖRTE, *Zur Lehre vom rund. Magengeschwüre* In. Diss. Strasburg 1875; LEUBE, *Deut. Arch. f. klin. Med.* XVIII., *Ziemssen's Cyclop.* VII., with references; L. MÜLLER, *Das corrosive Geschwür des Magens* Erlangen 1880, with full references; BÖTTCHER, *Dorpat. med. Zeitschr.* 1874; HAUSER, *Das chronische Magengeschwür* Leipzig 1883; WIKTOROWSKY, *Virch. Arch.* vol. 94. QUINCKE and DÄTTWYLER (*Mittheil. d. Vereins Schleswig-Holsteinscher Aerzte* 1880, *Deut. med. Woch.* 6, 1882) have produced gastric ulcers

in dogs by various methods, and find that in normal conditions repair is very rapid; whereas in anæmic or debilitated animals it is delayed. This observation entirely accords with clinical experience. Lesions of the gastric mucous membrane usually heal readily and rapidly; it is only when some local or constitutional condition impedes the process of repair that progressive digestion or solution of the injured tissue is set up, and the gastric ulcer assumes its typically chronic and intractable character.

461. **Tumors of the Stomach.** **Carcinoma** is by far the commonest and most important of the new growths affecting the stomach.

All cancers start in the mucosa, but very quickly extend to the submucosa (Art. 431); in this way it is frequently found that the main mass of the growth lies beneath the mucosa in the submucous stratum. Thence the disease invades the muscular and serous coats (Art. 431, Fig. 174 *A*). In the latter it usually spreads in the form of discrete nodules and nodes, which are perceptible from without, and follow the course of the lymphatic vessels. At a later stage it may invade the veins, giving rise to carcinomatous thromboses, which take the form of long flat elevations of the serous surface, lying chiefly about the pyloric end of the stomach.

The lymphatic glands situated behind the lesser curvature soon become enlarged, and are often transformed into huge cancerous nodes. The disease may likewise extend to the omentum and give rise to a general thickening of its tissue or to irregular tuberous growths. In other cases metastases occur in the peritoneum generally, and in the liver, lungs, etc. The liver is the commonest seat of the metastatic growths, the germinal elements being conveyed by the portal vein.

Gastric carcinoma most frequently takes the form of soft fungous tumors arising from the pyloric end and along the lesser curvature; tumors arising from the fundus and general or diffuse cancerous infiltration are more rare. When the tumor projecting into the cavity of the stomach has attained a certain size, its central parts usually break down and a carcinomatous ulcer is produced. Such an ulcer is distinguished by its raised rampart-like borders. Its floor is generally formed by the submucosa, which is thickened by fibrous hyperplasia or cancerous infiltration. The former is a result of chronic irritative inflammation.

The fibrous tissue of the muscular and serous coats is often the seat of extensive hyperplasia, causing the whole of the affected region of the stomach to appear thickened and indurated. A very similar appearance may be due simply to cancerous infiltration.

Occasionally the neoplastic tissue within the cavity of the stomach becomes entirely disintegrated, so that the surface of the ulcer appears smooth and level. When in such a case the stomach-wall is not visibly beset with nests and clusters of cancer-cells, but is simply indurated in consequence of fibrous hyperplasia, the affected region may wear the look of a simple non-malignant or fibroid induration. Cases occur in which no cell-nests are to be made out even when the tissue is micro-

scopically examined: and then the only evidence forthcoming as to the cancerous nature of the disease may be the metastic growths to which it has given rise.

462. Five chief forms of gastric cancer are distinguished according to their histological structure.

(1) **Medullary carcinoma** (Art. 173) takes the form of soft fungous excrescences or low rounded swellings, chiefly about the pyloric end of the stomach. As the central parts break down these growths give place to ulcers with raised borders, white and pulpy in appearance. The new growth starts in the gastric glands. Structurally it is distinguished by the presence of an extraordinary number of cell-nests or loculi, while the stroma is but slightly developed. Beneath the ulcer the wall of the stomach is nearly always indurated or infiltrated. This form produces numerous metastases.

(2) **Destructive adenoma** (adenocarcinoma, Art. 169) also gives rise to soft nodular growths, which presently break down and ulcerate. The neoplasm is distinguished by the presence of tubular gland-like structures, which often possess a simple cylindrical epithelium (Fig. 174 *A*, Art. 431), and thus closely resemble normal glands; hence the term adenoma. This close resemblance is however generally lost as the disease advances, and large cell-nests arise from the tubular structures, which are merely covered over with cylindrical epithelium, the interior consisting mainly of polymorphous cancer-cells. The stroma is not abundant, and is often infiltrated with small leucocytes. As the growth ulcerates its base almost always become indurated and thickened by fibrous hyperplasia or cancerous infiltration.

(3) **Scirrhous cancer** appears in the form of diffuse thickening and induration of the stomach-wall, especially the pyloric part of it. The pylorus itself is usually more or less constricted. The inner surface of the diseased region is covered partly with thickened mucous membrane, partly with the exposed and indurated fibrous tissue belonging to the submucosa. On section the various coats are distinguishable, but each is more or less thickened by fibrous hyperplasia. The author is of opinion that so-called scirrhus is often nothing but induration of the stomach-wall, partly cancerous and partly fibroid, left as a secondary result of the ulcerative disintegration of a soft cancer (Art. 173).

(4) **Colloid or gelatinous cancer** takes the form both of nodular swellings and of diffuse and wide-spread infiltration of the stomach-wall. In each form the neoplasm contains patches of transparent jelly-like appearance, or consists almost entirely of colloid substance. The growth often spreads to the peritoneum, and there speedily gives rise to large semi-transparent colloid growths, which are more or less richly supplied with blood-vessels. On microscopic examination it appears that the colloid masses are partly derived from the cancer-cells, partly from the fibrous stroma of the growth (Art. 173, Figs. 69 and 70). Colloid can-

cer may appear in very young patients, while the other forms are almost entirely confined to persons in the decline of life.

(5) **Squamous epithelial cancer** is rarely met with in the stomach. It affects the cardiac end and the neigboring parts of the œsophagus.

The **connective-tissue growths** of the stomach have very little pathological interest. A few cases of nodular sarcoma, fibroma, and myoma, have been recorded.

CHAPTER LIV.

THE INTESTINE.

463. **Introductory.** The intestinal part of the alimentary canal is that within which especially the assimilable parts of the food are absorbed, and so reach the lymphatics and blood-vessels. The intestine (according to some authorities) contains no new or specifically distinct variety of secreting glands, and its mucous membrane yields no specific secretions. On the other hand its absorbing surface is greatly increased by being thrown into a multitude of villi and valvular folds and tube-like crypts or pits.

The **epithelium** consists throughout of a single layer of cylindrical cells, the blood-vessels and lymphatics extending up to the lower surface of the epithelium.

The loose-textured connective tissue of the mucosa and submucosa expands at many points into a still looser reticulum, which contains lymphoid cells in abundance and so constitutes lymphadenoid tissue. This is aggregated into single nodules, the so-called **solitary glands** or follicles, or groups of these are agminated to form **Peyer's patches.**

It is scarcely needful to point out that it is from the mucous surface that the intestine is most exposed to injury. Matters constantly pass into it from the stomach which react harmfully on its tissues, and the mucous membrane is the first part to be attacked. The normal contents, if they stagnate and so become altered in their physical or chemical characters, may give rise to various morbid conditions. In other cases we must assume that specifically noxious matters enter the canal from the mouth, and that these may be the cause of certain intestinal disorders. Many such disorders are probably due to specific bacteria, and in some of them these have been actually demonstrated.

As regards the affections of the intestine which are traceable to the circulation, we need only remark that the intestinal mucous membrane like others is liable to œdema and hæmorrhage in the mucosa and submucosa, to fatty and mucoid degeneration of its epithelium, and to amyloid degeneration of its connective tissue.

There are however disorders of the intestine other than those connected with the mucous membrane, and affecting the viscus as a whole. The intestine forms a freely movable tube lying in the abdominal cavity; it is therefore subject to misplacements and displacements of the

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whole (or of its parts in relation to each other) which may give rise to serious disturbances of its function and may even imperil the integrity of its structure. Disease or injury may also affect the intestine from its serous or peritoneal surface.

464. **Congenital defects and misplacements.** Absence of the whole or of a large portion of the intestine is met with only in very ill-developed acardiac monsters. Minor deficiencies, constrictions, and occlusions, are somewhat commoner. The anal region is that which is oftenest imperfectly developed. The allantoid cloaca may persist, that is to say the intestine and the bladder open into a common chamber or orifice. In such cases the bladder is frequently unclosed and the lower bowel absent, so that the ileum communicates directly with the cloaca. In less-marked cases there is merely an imperfect separation of the rectum from the urogenital sinus, into which latter the genital and urinary canals open in the fœtus. The anus itself, which is developed from an invagination of the external skin, is wanting, and the condition is described as *atresia ani* or **imperforate anus:** and according as the lower end of the bowel is connected with the bladder, the urethra, or the vagina, the atresia is distinguished as vesical, urethral, or vaginal. When the rectum is completely separate from the urogenital sinus, although not in communication with the anal invagination, we have simple *atresia ani:* the rectum is usually ill-developed.

The formation of abnormal septa in the continuity of the intestine is much more rare than atresia of its anal extremity.

Abnormal shortness or length of the canal is on the other hand a much commoner anomaly.

As common perhaps is the existence of what is called **Meckel's diverticulum** (Art. 9). This is a cylindrical or flask-shaped appendage, attached to the ileum about a metre or more above the ileo-cæcal valve; it is a remnant of the omphalo-mesenteric duct. In rare cases it is connected by a cord with the umbilicus, and in still rarer cases it opens on the exterior just below the umbilicus. Its structure is the same as that of the small intestine.

When the abdominal wall is congenitally fissured or sacculated, coils of intestine may lodge in the openings so produced. A piece of intestine lodged in a sacculation of the peritoneum is spoken of as a **hernia** (Art. 465), and a coil or other portion which escapes to the exterior through an opening is called a **prolapse.**

But apart from these protrusions the intestine is very frequently misplaced, especially when some segment of it is abnormally short or long. Owing to its normally fixed position displacements of the colon are the most easily recognized. The cæcum, for instance, varies much in position; it may lie either below or above the line joining the anterior superior spines of the ilia. The level of the hepatic and splenic flexures differs much in different persons. The length of the sigmoid flexure

and of the transverse colon is very variable. In some cases the latter may be absent altogether, the ascending and descending portions lying side by side on the right of the abdomen.

Enterocystomata (ROTH, *Virch. Arch.* vol. 86) are structures allied to the congenital diverticula of the intestine. They are closed sacs filled with liquid, and exhibiting the same structure as the walls of the bowel. Two forms may be distinguished—(1) cysts due to the sacculation and abstriction of portions of an otherwise normally developed intestine: (2) cysts due to some abnormality of development in the fœtus. These latter may in reality be portions of the intestine of a rudimentary twin and therefore teratoid in character, or depend on the closure and separation of an anomalous diverticulum such as Meckel's. They may increase greatly in size from accumulated secretion, and then become displaced from their original site.

465. **Acquired deformities and displacements.** Abdominal hernia or 'rupture' in the stricter sense implies the escape from the abnominal cavity of some part of its normal contents either to the exterior or into some other cavity of the body.

In **external hernia** some viscus which is covered with peritoneum escapes outwards through a normal opening which has become abnormally dilated, pushing before it the subperitoneal structures and the skin. The protruded layer of the parietal peritoneum forms the **hernial sac.** It can be absent only when the peritoneum has been torn or when the displaced viscus is extraperitoneal (such as part of the bladder or cæcum) and protrudes directly through some opening in the fascia or muscles of the abdominal wall. The other tissues which are forced outwards with the hernia are spoken of as the **accessory coverings** of the hernial sac. The inner layer or covering consists of the subperitoneal cellular tissue, which is usually thickened and toughened (peritoneal fascia). In femoral and inguinal hernia the true fascia (fascia propria) comes next, and is continuous with the fibrous structures bounding the orifice in the abdominal wall through which the hernia has escaped. At first the hernial sac is simply globular or saucer-shaped; when fully developed it is in general flask-shaped. The narrower part of the sac where it is gripped by the structures of the orifice is called its **neck.** The peritoneum is drawn into radial folds as it passes towards the neck of the sac.

The **contents of a hernia** are very various. Most commonly they consist of a part of the omentum or small intestine, less commonly the cæcum or colon, and still less commonly other viscera such as the ovaries, bladder, stomach, liver, etc. Very large ruptures, such as occur in the inguinal region, may include the greater part of the contents of the abdomen, more especially the bowels. When a portion only of the intestinal wall or Meckel's diverticulum is included we have a case of what is called **Littré's hernia** (LITTRÉ, *Mémoires de l'acad. royale* 1700).

In a large number of hernias the sac is already formed before the viscera escape. Thus inguinal hernia may occur by the passage of the intestine into the persistent vaginal process of the peritoneum which is continuous with the tunica vaginalis of the testicle. This is usually the case in what is called infantile or congenital hernia.

Hernia may also arise in consequence of some external stretching force by which the peritoneum is dragged outwards. Thus a lipoma growing in the septum crurale, and pressing outwards as it increases in size, may drag upon and sacculate the peritoneum which is firmly attached to the septum. Something of the same kind takes place in umbilical hernia.

Lastly, some local diminution of the resistance of the abdominal wall, or the giving way of muscles or fasciæ and the relaxation of the peritoneum, may cause the latter to become sacculated under the pressure of the respiration.

The following varieties of external hernia may be distinguished.

(1) **Inguinal hernia.** This takes place in the groin, and is due either to the congenital patency of the vaginal process of the peritoneum after the descent of the testicle, or to a secondary protrusion of the peritoneum in the inguinal canal. In **oblique** or external inguinal hernia the neck of the sac passes down the canal from the internal to the external ring; in **direct** or internal inguinal hernia the the peritoneum is pushed from within directly through the external ring. In oblique hernia the orifice of the sac lies to the outer side of the internal epigastric artery, in direct hernia the orifice lies to the inner side of the artery. Inguinal hernia may reach a large size and contain the greater part of the bowels. It is the commonest of all varieties, especially in men.

(2) **Femoral or crural hernia.** This is due to the protrusion of the peritoneum beneath Poupart's ligament through the opening closed by the septum crurale and traversed by the great femoral vessels. It is a common variety, especially in women.

(3) **Obturator hernia.** In this the sac passes with the obturator nerve and artery through the obturator or thyroid foramen of the innominate bone.

(4) **Ischiatic hernia.** Here the protrusion is through the ischiatic notch beneath the glutæus maximus: it is rare.

(5) **Perineal hernia.** Here the sac escapes between the anterior fibres of the levator ani: it is also rare.

(6) **Umbilical hernia.** This is either congenital, consisting of a protrusion through the unclosed umbilical ring into the root of the cord (Art. 9), or acquired, and is then due to the separation of the fibres of the linea alba at the umbilicus and dilatation of the orifice so formed. It may contain intestine or omentum only. The acquired form is most commonly met with in women who have borne children.

(7) **Ventral hernia.** This is due to the general relaxation or stretching of the fibrous structures of the front of the abdominal wall, so that the peritoneum protrudes between the muscles which are thrust asunder.

466. When a hernia is once established, further changes in the parts usually follow. The hernia may increase in size by the inclusion of more of the abdominal contents. The sac stretches and becomes thinner, or

new portions of the peritoneum are dragged into it. In consequence of the slight mechanical lesions to which the hernia is exposed a certain amount of inflammation is usually set up. The sac thereby thickens and the folds of peritoneum at the neck cohere so that the channel of communication between the sac and the abdominal cavity becomes thick-walled and inextensible. The serous covering of the included intestine, and its mesentery, and of the omentum, become thickened in like manner. Lastly, adhesions may be set up between different parts of the sac, or between different loops of intestine and the sac-wall. The omentum is very apt to adhere to the sac.

These changes very rarely indeed lead to cure by the closure and obliteration of the empty sac; on the contrary they usually make matters worse. The thickening and adhesions of the serous surfaces diminish by degrees the mobility of the included viscera. The neck of the sac becomes narrower, constricting its contents more and more. At length the contents can no longer be returned to the abdomen; the reducible hernia has become irreducible. When the contents of a hernia (reducible or not) are so constricted or compressed that the included intestine becomes impervious and its circulation seriously impaired, the hernia is said to be strangulated or incarcerated.

Strangulation or **incarceration** may be due to simple narrowing of the neck of the sac or of the orifice through which it passes; or it may arise from inflammatory constriction of the intestine within the sac; or a loop of intestine within the sac may slip between two edges or bands of false membrane or into a gap in an included piece of omentum; or a piece of omentum may be squeezed into the neck of the sac and so compress the intestine; and so on.

A narrow orifice, a band of false membrane, etc., may strangulate a loop of intestine without any abnormal distention of the latter by its contents. This may happen suddenly, for example, when the intestine is forced through a narrow orifice by an unusually deep respiration. This is sometimes referred to as 'elastic' strangulation. More often however the strangulation is dependent on some increase of the intestinal contents, the orifice of the sac being narrow; this may be called 'fæcal' strangulation. The fæces accumulating in one coil of the intestine within the sac compress the other included coils in such a way as to nip them; stoppage or stasis of the contents takes place and the peristaltic movements are interfered with (Kocher). Presently the first coil is nipped in like manner, as the distended intestine presses up against the narrow neck of the sac.

When a coil of intestine or a part of the omentum is constricted and strangulated, disturbances of the circulation almost always take place. The venous efflux is impeded, and engorgement, transudation, and hæmorrhage result. The coil becomes purple and swollen, and liquid gathers in the sac; and these factors conspire to intensify the strangulation.

If nothing is done the intestine sooner or later becomes gangrenous, and violent inflammation of the hernial sac ensues. The intestine becomes discolored, turning brown or bluish-black; at the point of strangulation it is paler and somewhat grayish. Presently perforation takes place, and at the boundary between the living tissue and the dead, that is at the inner border of the strangulating constriction, definitive suppuration is set up.

467. Incarceration of the intestine, with obstruction and stasis of the fæces, may occur within the abdomen as well as in an external hernia. This has been called internal strangulation or **intestinal obstruction**.

In the first place it must be remembered that within the peritoneal cavity there are pouches or recesses of peritoneum not visible outwardly, which are either normal or dependent on congenital anomalies. In these pouches coils of intestine may become incarcerated as in external hernias, and they are sometimes spoken of as cases of **internal hernia**. Among such pouches we may mention the lesser or omental sac of the peritoneum bounded by the stomach, pancreas, liver, and spleen, and communicating with the greater sac through the foramen of Winslow; the duodeno-jejunal fossa, between the upper part of the mesentery and the spine; the subcæcal fossa, on the mesial side of the cæcum; and the intersigmoid fossa, beneath the mesocolon of the sigmoid flexure. Coils of intestine may slip into and be incarcerated in any of these pouches. The duodeno-jejunal fossa may indeed enclose the whole of the small intestine (retroperitoneal hernia).

In rare instances sacculations of the diaphragm may contain coils of intestine, giving rise to **diaphragmatic hernia**. Cases are more common in which abdominal viscera escape into the thorax through actual rents in the diaphragm (THOMA, *Virch. Arch.* vol. 88).

Sometimes in consequence of plastic inflammation false membranes and adhesions are formed within the abdomen, and if these enclose gaps or pouches, internal incarceration may occur. If the opening through which the coil of intestine slips is narrow, or if the coil is nipped, stasis and all the other symptoms of strangulation may be produced. The like may happen when the omentum or the mesentery contains abnormal perforations or gaps.

Another cause of intestinal obstruction is twisting of the bowel on itself, or **volvulus**. It can occur only in the more movable parts of the tract, and is due partly to peristaltic movements, especially when the tube is very unequally distended, and partly to external violence, such as a blow on the abdomen. The twist occurs at the mesenteric attachment, the two limbs of the coil crossing each other over the mesentery. The channel of the intestine is occluded and the mesenteric circulation stopped. Untwisting is prevented by the weight of the distended coil and the pressure of the rest of the abdominal contents.

Twisting of the sigmoid flexure or of the small intestine may result

in a kind of knotting between the two, the attached end of the twisted coil of one part becoming encircled by a loop of the other.

468. **Stenosis** and **atresia** are not infrequently the result of inflammation of the wall of the intestine itself. The serous coat may become inflamed, and so indurated, cicatrized, and contracted; or ulcerative inflammation of the mucous membrane may result in the formation of new fibrous tissue, which subsequently contracts. Carcinomatous ulcers, the floors of which tend to become indurated and contracted (Art. 478), may have the same effect; while tumors and other growths developing within the canal or pressing on it from without may obstruct and ultimately occlude it.

Dilatation of the intestine is most commonly due to retention of fæces, or other contents such as flatus. Tumors, and abnormal relaxation or softness of the wall, may also give rise to dilatation.

Usually all the coats are dilated together; sometimes, however, the muscular structures are here and there pushed aside, and the mucous and submucous coats bulge through, producing sacculations or **false diverticula** of various sizes. Sacculations may also be due to the bulging of the wall in its whole thickness.

Perforation of the bowel is in general due to some localized textural change, especially to uleration of the mucous surface, necrosis, or softening occasioned by suppuration in the neighborhood of the part. Perforation may of course be caused by mechanical violence.

The result of perforation, unless the lips of the wound immediately close, is local or general peritonitis due to the escape of fæces. The peritonitis is localized when by previous inflammation adhesions have been set up around the point of perforation. If fæces escape into the portion of the peritoneum so circumscribed a fæcal abscess is produced; this may break either outwardly or into another part of the intestine.

469. A not uncommon kind of displacement or dislocation of the intestine is that known as **intussusception**. In this a higher part of the bowel slips into or is invaginated by a lower, rarely the reverse. Recent intussusceptions are most frequently met with in the small intestine in young children, especially in those who have died of cerebral or intestinal affections.

The extent of the invagination varies much. Where the intestine is very loose and movable a very considerable length of it may be involved. Thus, for example, the lower portion of the ileum with the cæcum may be thrust into the colon, and work downwards until the ileo-cæcal valve reaches the sigmoid flexure or even the rectum.

The mesentery being severely dragged upon and its vessels compressed, the invaginated portion of the bowel becomes highly hyperæmic and œdematous. Presently inflammation is set up, and this may lead to adhesions between the enclosed and enclosing segments; necrosis and gangrene usually ensue. It is a comparatively favorable issue when the

whole of the invaginated segment necroses and separates so as to be cast off completely; the upper portion becoming adherent and its channel continuous with that of the lower, recovery may and in some cases does take place.

The cause of intussusception is not certainly made out. According to LEICHTENSTERN it depends on paresis or partial paralysis of a limited portion of the bowel. When this occurs an energetic peristaltic movement of the portion immediately above may thrust the latter into the flaccid or paralyzed portion; and then continued peristalsis rapidly increases the invagination.

Prolapse of the bowel implies its escape through some normal or abnormal opening. The anus is the only possible normal opening, and through it the rectum may protrude.

Prolapsus reti (or *ani*) occurs during violent straining at stool, especially when the intestine is relaxed by chronic inflammation. The protruding bowel forms a kind of tumor covered with mucous membrane; it often becomes inflamed or gangrenous, particularly in cases where by adhesions or constriction the prolapse has become irreducible.

470. **Non-specific inflammations.** The varieties of inflammation described in Arts. 420–428 are all met with more or less frequently in the intestine. Catarrhal inflammation (**intestinal catarrh**) or enteritis is especially common. The catarrhal secretion may be serous, mucous, purulent, or of some intermediate kind. In the colon the amount of mucus secreted is sometimes enormous. Catarrhal enteritis is usually an acute disorder and ends in complete recovery. But in many cases the acute forms as well as the chronic leave behind them permanent structural change in the intestine.

Even in the milder forms the connective tissue lying between the crypts of Lieberkühn becomes infiltrated with liquid and extravasated cells. The epithelial cells pour out an excessive quantity of mucus, and become loosened from their sub-structures or fall away altogether. According to BÖHM desquamation of the epithelium is characteristic of poisoning with arsenic and with some substances of the muscarin-group. If this process goes too far or lasts too long, the lost epithelium fails to be reproduced and the intestinal wall becomes atrophied. When slight such atrophy is not apparent to the unaided eye, or at most it gives the wall an unusually smooth and level appearance. Under the microscope the glandular layer of the mucosa is seen to be thinned and wasted. The crypts may lose a half or two-thirds of their depth, and the villi of the small intestine are slender and stunted.

After an attack of ulcerative catarrh, in which not only the epithelium but the underlying connective tissue is injured or destroyed (Art. 421, Fig. 167), the atrophy is usually much more marked. The ulcerated portion of the bowel is covered with mucus, pus, and whitish granulations and shreds of tissue; these last are simply the necrosed remains

of the glandular layer, which has become infiltrated and broken down. The ulceration is in fact associated with diphtheritic necrosis of the mucous membrane, and in such cases not only the upper layer but the whole of the glandular mucosa may perish, leaving the muscularis mucosæ covered with nothing but a film of nucleated connective tissue (Art. 417, Fig. 165).

The muscularis mucosæ as a rule is very slightly altered. Its unstriped fibres are only in rare cases found to be thinned, or atrophied, or fatty. The submucosa is generally unchanged; when the ulceration goes deep it may be infiltrated with leucocytes or thickened from subsequent fibrous hyperplasia.

The lymphadenoid follicles are in the slighter forms of catarrh but little affected; at most they are somewhat enlarged. Sometimes in suppurative or ulcerative inflammations they are more markedly altered, and may then perish by suppuration, giving rise to what is called follicular catarrh. They may leave behind small pitted ulcers known as **follicular ulcers**.

Catarrh ending in **atrophy** is commonest in the large intestine, and especially in the cæcum. NOTHNAGEL found that in 80 per cent of the adults he examined there were traces of atrophy in the large intestine, at times confined entirely to the cæcum. The ascending colon came next as regards frequency, and then in diminishing order the lower part of the ileum, the remainder of the colon, the upper part of the ileum, and the jejunum. In children intestinal atrophy is often met with, following on acute and subacute, as well as on chronic, catarrh.

The muscular coat is usually unaffected, but here and there it may be atrophied, or in catarrh from venous engorgement it may be hypertrophied (NOTHNAGEL). It is not very liable to degeneration, but sometimes as in phthisis it is found to be fatty (WAGNER). Lastly, there is a congenital form of atrophy, a hypoplasia of the muscularis which is not made up in later life (NOTHNAGEL).

In chronic catarrh atrophy is occasionally associated with the development of hyperplastic growths. They take the form of indurations of the submucosa or polypous excrescences rising from the mucosa. When fully developed these last consist of fibrous tissue enclosing a few remains of glandular structures, which here and there are degenerated into closed **cysts**.

Diphtheritic and **croupous inflammations** occur chiefly in the colon and in the lower part of the small intestine. The diphtheritic form closely resembles ulcerative catarrh, and is not easily distinguished from it. The intensely red and swollen membrane is covered with a thin but tough film or a broad continuous slough (Art. 472). This form is sometimes at least due to specific infection.

Croupous inflammation is rarely very extensive, though now and then considerable portions of the bowel are found to be red and highly

swollen and covered with a thin flaky fibrinous deposit. Small circumscribed croupous exudations are more frequently met with, associated with ulcerative catarrh and diphtheritic necrosis.

References:—WAGNER, *Arch. d. Heilk.* II. (1868); KUNDRAT, *Gerhardt's Handbuch. d. Kinderkr.* IV.; WHITEHEAD, *Brit. med. Journ.* 1, 1871; WOODWARD, *Med. and surg. history of the War of the Rebellion* Part II. vol. 1 (medical history) Philadelphia 1879 (with references); DAMASCHINO, *Maladies des voies digestives* Paris 1880; KUSSMAUL and MAIER, *Arch. f. klin. Med.* IV.; SCHWARCK, *Croup and Diphtheritis d. Darmcanals* In. Diss. Bonn 1880; LEUBE, *Ziemssen's Cyclop.* VII.; NOTHNAGEL, *Zeitschr. f. klin. Med.* IV. (1882).

471. Inflammations of the bowel have received various names according to the particular parts affected. Several of these local inflammations exhibit peculiarities depending on the anatomical relations of their respective seats. The chief of them are the following.

(1) **Duodenitis**, or inflammation of the duodenum, is usually associated with inflammation of the stomach. It not infrequently leads to obstruction at the mouth of the bile-duct, and thereby to retention of bile and jaundice (**catarrhal jaundice**).

The duodenum is also the seat of simple or perforating ulcer corresponding to perforating ulcer of the stomach, and like it dependent on digestive corrosion (KRAUS, *Das perforirende Geschwür im Duodenum* Berlin 1865).

(2) **Ileitis**, inflammation of the ileum, is often marked by the swelling and prominence of the solitary and agminated follicles. The former appear as reddish or grayish protuberant nodules, the agminated follicles as flat elevations, grayish-red or pink in color and pitted with numerous little depressions. When these follicles break down they leave behind them follicular ulcers.

(3) **Typhlitis** and **perityphlitis** imply inflammation of the vermiform appendage and the parts around it.

The vermiform appendage is peculiarly adapted to catch and retain substances passing through the cæcum. Matters which have been swallowed—such as grape-seeds, apple-pips, cherry-stones, and the like—and fæces, may accumulate in the appendage and set up inflammation. Sometimes these become crusted over with phosphates and carbonates and so form fæcal concretions or calculi (**entroliths**, Art. 479). The inflammation thus set up may extend to all the coats of the appendage and then attack the contiguous structures, and in this way necrosis and gangrene with perforation may be caused. The issue differs in different cases. It is comparatively favorable if the inflammation continues to be circumscribed, while the exudation is moderate in amount; protective adhesions and false membranes may thus be formed about the affected spot. It is very unfavorable when perforation takes place before adequate adhesions are formed; fatal peritonitis is nearly always induced. When perforation takes place into a part of the peritoneum shut off by

adhesions a burrowing fæcal abscess is produced, which may burst internally or externally. Sometimes the appendage is entirely obliterated by adhesive inflammation; but if the inner or intestinal end becomes closed while the remainder continues to be patent, the natural mucous secretion may collect in the latter and distended it into a **cyst.**

Typhlitis and perityphlitis are sometimes due to the extension by continuity of inflammation already existing in more distant parts of the cæcum or colon. Tuberculous and typhoid ulceration localized in the vermiform appendage may give rise to dangerous lesions.

(4) **Colitis,** or inflammation of the large intestine, is somewhat common. Its peculiarities have already been referred to (Art. 470). The exciting causes are very various. Sometimes it is due to the stoppage and accumulation of fæces forming hard masses or **scybala,** sometimes to septic infection, sometimes to a specific poison as in dysentery (Art. 472).

(5) **Proctitis** is an inflammation of the rectum. In many points it resembles inflammation of the vermiform appendage. Foreign matters and stagnating fæces are frequently the exciting agents; but disturbance of the circulation in the hæmorrhoidal veins may likewise end by inducing inflammatory change in the bowel.

Proctitis often results in the formation of ulcers, and of fibroid hyperplasia taking the form of induration of the rectal wall or of polypous excrescences. The inflamed surface is usually covered with a muco-purulent exudation. When the inflammation and ulceration extend deeply into the tissues of the wall of the bowel, the surrounding connective tissue becomes infiltrated and hyperplastic, or breaks down into abscesses containing fœtid pus (**periproctitis**). The ulcers of the mucosa and submucosa come in this way to communicate with burrowing sinuses and fistulous tracks extending into the surrounding parts, which are called incomplete or blind **internal fistulæ.** Circumscribed or enclosed periproctal abscesses may break outwardly, and then constitute blind **external fistulæ.** Fistulæ which communicate both with the rectum and with the exterior are called complete rectal fistulæ or **fistulæ in ano.** They become covered with a kind of factitious mucous membrane. Fistulæ occasionally communicate with the bladder or vagina.

Specific poisons like those of syphilis, tuberculosis, and dysentery, and cancer in the ulcerative stage, may give rise to morbid changes of a similar kind. There may even be periproctitis without any antecedent rectal ulceration, especially in connection with pyæmia, typhoid, acute rheumatism, and puerperal septicæmia.

References on typhlitis and perityphlitis:—MATTERSTOCK, *Gerhardt's Handb. d. Kinderkr.* VI.; BIERHOFF, *Arch. f. klin. Med.* XXXVII.; CORNIL, *Arch. de physiol.* 1873; WÖLFLER, *Arch. f. klin. Chir.* XXI.; STEINER, *Zur path. Anat.*

d. Wurmfortsatzes Basle 1882 ; CRISP, *Trans. Path. Soc.* 1858 (foreign bodies in the appendage).

472. **Specific inflammations. Dysentery** is an inflammatory affection of the large intestine, due to the action of a specific virus. The exact nature of the virus is unknown, but it is probably bacterial. The affection is epidemic, endemic, or sporadic in its occurrence. The changes set up in the intestine closely resemble certain non-specific inflammations of the colon, especially such as depend on retention of fæces or accompany septic poisoning. For this reason the exact significance of the term dysentery is not easily fixed, inasmuch as it is often impossible to say from the post-mortem appearances whether these are the result of specific infection or not. Moreover it is not impossible that the so-called endemic dysentery of different countries may be really due to different specific poisons.

The intensity and extent of the dysenteric inflammation varies in different cases. It may be restricted to the rectum, sigmoid flexure, and descending colon, or it may reach up to or a little beyond the ileocæcal valve. Often too in the same case the various parts of the tract are variously affected.

In recent cases the mucous membrane is highly congested and swollen, and generally beset with minute extravasations of blood. The epithelial surface is overlaid with a glairy blood-streaked mucus. This presently becomes more slimy and blood-stained, and interpersed with the flaky fibrinous shreds and films (described in Art. 470) which indicate the beginning of superficial necrosis of the mucous membrane. Soon the necrosis is made sufficiently evident by the appearance of erosions and losses of substance.

We might perhaps distinguish a catarrhal and a diphtheritic form of dysenteric inflammation, but in practice the one passes insensibly into the other and the distinction is inappreciable. In slighter cases the necrosis and loss of substance are at first merely superficial (Fig. 177 *f*); but the deeper structures are successively attacked, and in severe cases the greater part or the whole of the glandular layer of the mucous membrane at particular spots may perish. The necrotic tissue is reduced to a turbid granular mass, in which the structural elements and the nuclei of the cells soon cease to be recognizable. The parts which undergo necrosis seldom cover any great extent of surface, and are often confined to the prominent ridges and folds of the mucous membrane; these look dirty-gray or black, while the intervening parts are still livid or dark-red. In other cases the necrotic tissue takes the form of a flaky more or less adherent coating, or more rarely of broad continuous sloughs. The underlying tissue is in all cases densely infiltrated with cells (d_1). The infiltration may extend through the entire thickness of the submucosa (e), and may at length invade the muscular layers.

The lymphadenoid follicles take part in the process, and frequently ulcerate. Occasionally the mucosa is undermined by suppuration beneath it, and in this way broad patches of the tissue are separated and cast off.

When the mucosa is removed, open ulcers are of course left behind. These vary much in their depth and extent; sometimes over a great part of the bowel the mucous membrane remains only in narrow strips and islands.

The affection may come to a standstill at various stages of its course, and repair then begins. The slighter cases, in which but little substance is lost, are naturally the readiest to heal; but a certain amount of atrophy of the mucosa always remains. When the ulcerative process has gone further, atrophic cicatrices are left to mark the site of the injury. In

FIG. 177. SECTION THROUGH THE COLON FROM A CASE OF DYSENTERY.
(*Hæmatoxylin staining:* × 25.)

a, mucosa.
b, submucosa.
c, muscularis.
d, interglandular, and
d_1, subglandular infiltration of the mucosa.
e, infiltration of the submucosa.
f, superficial glandular layer, infiltrated and separating.
g, ulcer, the floor of which is infiltrated.

severe cases accompanied by great destruction of tissue, in which the acute specific inflammation is succeeded by chronic inflammation, the whole structure of the bowel is altered in a remarkable way. Over broad areas the glandular layer is almost or altogether absent; the deeper layers of the mucosa and submucosa look coarse and dense and indurated; the connective structures are hyperplastic; and the other coats are likewise tough, thickened, and unyielding. The channel of the intestine is usually narrowed, often so much so that a finger can hardly be introduced. The mucous membrane is only recognizable in isolated patches here and there, and these not infrequently assume the form of papillary or polypous outgrowths from the general surface.

In the scarred and indurated portions of the bowel the submucous connective tissue (and that of the mucosa if any remains) is thicker and denser than normal, and often shows signs of cellular infiltration. There may be no trace of the intestinal glands remaining, or only their lower parts; while in some places portions of the glandular layer which have been separated and abstricted by the invading fibrous tissue may become distended with secretion, and form small cysts lined within with cylindrical epithelium. The muscular coats are traversed by dense bands of coarse fibrous tissue. A certain amount of chronic inflammation, accompanied by muco-purulent discharge, is often kept up long after the acute disorder is at an end; this constitutes what is sometimes called chronic dysentery, or by the older authors **cœliac flux**.

The author had the opportunity of examining certain cases in which epidemic dysentery had proved fatal in an early stage, and was able to demonstrate the presence of multitudes of micrococci in the affected tissues. They were found not only in the necrotic patches, but also in the neighboring unattacked portions of the mucosa. They lay partly beneath the glands of the mucosa, partly in the lymphatics of the submucosa: that is to say in tissue which was still to all appearance sound. In these cases it would appear that the micrococci were concerned in the causation of the disease. PRIOR (*Cent. f. klin. Med.* 17, 1883) records similar observations. In other cases which seemed precisely similar no micrococci could be discovered. For example, none were found in the case of the five natives of Tierra del Fuego who died of dysentery at Zurich in March 1882 (compare SEITZ, *Virch. Arch.* vol. 91).

473. **Epidemic** or **Asiatic cholera** is characterized anatomically by the presence of an acute inflammation extending over the whole of the intestine, accompanied by an enormously copious transudation of liquid through the mucous membrane.

In cases which prove fatal in the first two or three days the bowel is found to contain a great quantity of a turbid grayish inodorous alkaline liquid, often mingled with minute shreds and flakes—the so-called 'rice-water' stools. The mucous membrane is moist, pink, injected, and swollen. Sometimes the serous surface is dull or opaque. The epithelium separates within a few hours after death. The follicles of the small intestine are swollen, and gray or bright pink in color. Apart from the epithelial desquamation which is mainly a post-mortem phenomenon, microscopic examination reveals only a somewhat intense cellular infiltration of the mucosa and submucosa, and sometimes even of the serous coat.

When death does not occur till a later stage of the disease, the appearance of the intestine is notably different. The contents are scanty and less liquid, and at the same time they show more signs of the presence of bile. The mucous membrane is pale or slate colored, or it may be injected and beset with minute hæmorrhages. Ulcers occur, especially in the colon and lower part of the ileum. Sometimes the large intestine has almost the same look as in dysentery (Art. 472).

The special virus of cholera is as yet unknown.

KOCH and others have found peculiar bacilli in the intestinal mucous membrane of the cholera patients, but they have failed to reproduce the disease in animals by inoculation or otherwise. The experiments and observations hitherto made leave the question of the genesis of the disease unsettled. For summaries of the reports of the French and German Commissioners sent to Egypt in 1883 see *Practitioner* (March 1884) and *Brit. med. Journ.* (2, 1883 and 1, 1884).

474. **Typhoid** (or enteric) **fever** is an infective disease, due (according to KLEBS, EBERT, and KOCH) to the invasion of a specific bacillus (Art. 206).

The morbid changes in typhoid appear chiefly in the lower part of the ileum and the upper part of the colon; they are seldom met with

FIG. 178. SECTION THROUGH THE MARGIN OF A PEYER'S PATCH FROM A CASE OF TYPHOID FEVER.

(*Aniline-brown staining:* × 15.)

a, mucosa.
b, submucosa.
c, internal muscular coat.
d, external muscular coat.
e, serous coat.
(a_1 b_1 c_1 d_1 e_1, the same layers infiltrated and swollen).
f, crypts cut through transversely.
g, lymphadenoid follicles.

much higher or much lower in the intestine. The changes consist essentially of a necrotic inflammatory infiltration of the follicular structures and the parts around them, accompanied by a catarrhal inflammation of the rest of the mucous membrane.

In the first few days of the attack the mucous membrane of the lower part of the ileum and its agminated glands of Peyer's patches are intensely congested and uniformly swollen. Soon the swelling of the patches becomes more marked, raised and winding ridges not unlike the cerebral evolutions in miniature appearing on their surface. The swelling extends more or less quickly over the whole of each patch, so that it

has in general the look of a raised bed or garden-plot projecting above the general surface. When the swelling is at its height the ridges are generally levelled up as it were, and are no more distinguishable: the surface of the patch is then smooth or pitted with minute depressions corresponding to the sites of the individual follicles. The solitary follicles form rounded nodules by virtue of the same process.

When this stage (of swelling) is complete the patches and follicles, which at first were bright-red in color, become pale and creamy-white.

The swelling of the patches and follicles is chiefly due to the extreme cellular infiltration of the mucosa (Fig. 178 a_1) and submucosa (b_1). The glands (f) of the mucosa are thereby thrust assunder and displaced, and the villi are likewise infiltrated and swollen. The submucosa underlying the patches is uniformly infiltrated (b_1). In the earlier stages the several follicles (g) within the infiltrated region are still distinct and recognizable, but they are presently merged and lost in the general assemblage of lymphoid cells and leucocytes, extravasated and other.

The muscular and serous coats (c_1 d_1 e_1) are also invaded by the extravasated cells, though in a less marked degree.

The number of swollen patches and follicles varies much. Often but a small number or even a single one is markedly affected; while in other cases the affection extends upwards to the jejunum or downwards to the anus.

In the second week of the disease partial disintegration and necrosis of the swollen patches usually sets in. The disintegration attacks the whole of the central part of the patch, or two or more parts of it simultaneously. The surface quickly assumes a frayed or ragged appearance and becomes yellow or brown from the action of the bile. Gradually the disintegrated tissue or slough becomes loosened at its base and edges from the surviving structures, and in a few days is cast off.

After the separation of the sloughs, an erosion or **typhoid ulcer** is left, the floor of which generally looks smooth and clean. The borders of the ulcer are at this stage still swollen and infiltrated.

The ulcers usually remain coextensive with or very slightly overpass the area of the infiltrated patches and follicles; they rarely invade the tissue beyond. Cases however occur in which, especially around the ileo-cæcal valve, extensive tracts of mucous membrane are attacked and disintegrated by the advance of the ulcerative process. In the vertical direction it seldom goes beyond the mucosa and submucosa. It is only when the infiltration of the muscular coats has been extreme that they too break down and ulcerate. In exceptionally severe inflammation the serous coat also may be attacked, but never to the same extent as the overlying layers; perforation and fatal peritonitis may occur in such a case.

The processes of absorption and repair begin at various stages of the disease. If no necrosis takes place, the swelling of the patches goes

down as the infiltrated material is absorbed: the patches thereupon become less stiffly turgid, and once more hyperæmic. Red corpuscles escape from the damaged vessels, and the tissue takes on a red or blood-stained tint which presently turns to a slaty gray. The infiltrated borders of the typhoid ulcers become reduced and softened and hyperæmic by the same steps. Often enough considerable hæmorrhage ensues, leading not only to hæmorrhagic infiltration of the tissue but to actual escape of blood into the intestinal canal. As the healing process goes on the softened and overhanging borders of the ulcer become adherent to the floor; the latter is gradually covered over with delicate granulations, and soon receives an investment of epithelial cells.

The site of a former typhoid ulcer appears for a long time after as a smooth shallow depression, devoid of glands and follicles, slaty-gray in color, and situated in the midst of a Peyer's patch itself discolored in like manner.

The characteristic inflammation of the lymphadenoid structures of the intestine in typhoid is sometimes accompanied by an inflammation of the corresponding mesenteric glands. They are at first red, swollen, and œdematous Art. 336); but as the accumulation in them of leucocytes and lymphoid elements becomes more marked they take on a light-gray tint. The swelling either subsides from re-absorption of the infiltrated matters, the gland becoming soft and hyperæmic; or it terminates in partial necrosis, and opaque grayish patches appear within the substance of the gland. These patches may likewise be absorbed at a later stage, but they often become caseous or calcified. The spleen is usually swollen, and inflammation of the throat, especially affecting the follicular structures of the pharynx, is not an uncommon accompaniment.

With regard to the bacillus of typhoid see the references in Art. 206; and also EBERTH, *Virch. Arch.* vol. 83, *Samml. klin. Vorträge* no. 226; KLEIN, *Report of Med. Off. Loc. Gov. Board* 1875; W. MEYER, *Untersuch. üb. d. Bacillen d. Abdominaltyphus* In. Diss. Berlin 1882; WERNICH, *Zeitschr. f. klin. Med.* IV., V.; FRIEDLÄNDER, *Sitzungsber. d. physiol. Gesell. zu Berlin* 1881; COATS, *Brit. Med. Journ.* 1, 1882; CROOKE, *ibid.* 2, 1882; LETZERICH, *Arch. f. exper. Path.* XIV., *Aetiologie d. Typhus abdominalis* Leipzig 1883; GAFFKY, *Mitth. a. d. k. Gesundheitsamte* Berlin 1884.

475. **Tuberculosis** of the intestine has already been considered in Art. 428, so far at least as the minuter tuberculous tissue-changes are concerned. It is one of the commonest of intestinal diseases, and chiefly attacks the lymphadenoid structures. The neighborhood of the ileo-cæcal valve is the region most frequently affected, but often enough the whole of the large intestine down to the anus becomes tuberculous.

At first a little nodule covered with epithelium protrudes from the surface of a Peyer's patch or over a solitary follicle. After a time the centre of the nodule becomes pale-yellow, indicating that necrosis and caseation have begun. The caseous parts break down and a **tuberculous ulcer** (Fig. 179 *h*) with infiltrated borders is formed. The ulcer is minute, but soon enlarges as it coalesces with others formed

in like manner, while new foci of disintegration appear in its gradually advancing borders.

Ulcers of any great size are usually very irregular in their outline. Some are rounded, but more are oval or at least elongated, the longer axis being transverse to the axis of the bowel: others again are sinuous and spreading.

The borders are infiltrated, but in the larger ulcers not uniformly so. The gray or reddish raised edge is here and there beset with yellow nodules, and characteristic gray and yellow nodules appear on the floor. The depth of the ulcer is irregular, and sometimes small islands of undestroyed mucous membrane rise as grayish-red protuberances from its floor.

Where the ulceration is extensive, not only are the mucosa and sub-

FIG. 179. TUBERCULOSIS OF THE LARGE INTESTINE.

(*Bismark-brown staining:* × 80.)

a, mucosa.
b, submucosa.
c, internal muscular coat.
d, external muscular coat.
e, serous coat.
f, solitary follicle.
g, cellular infiltration of the mucosa.
h, tuberculous ulcer.
h_1, tuberculous abscess.
i, recent or gray tubercle.
i_1, caseous or yellow tubercle.

mucosa attacked but the muscular and at length the serous coats are invaded by the tuberculous infiltration. On the serous surface the gray tubercles appear in groups or beaded rows, the membrane in the neighborhood being red and injected.

Only in rare cases does tuberculous ulceration come to a stand-still and issue in cicatrization. As a rule it advances steadily, involving more and more of the bowel until the patient dies.

476. **Syphilis of the intestine.** Apart from the mucous patches frequently met with about the anus in syphilitic patients (Art. 379), there is a form of ulceration of the rectum also due to syphilis and occurring chiefly in women. It extends three or four inches up the bowel, and is usually separated by a distinct line from the healthy mucous membrane. The ulcerated surface is remarkably uneven and irregular, and is generally interspersed with strips and patches of more or less undermined epithelial tissue. The borders of the ulcer are undermined in like manner. This appearance is due to the fact that the inflammation attacks chiefly the submucosa, and destroys it more rapidly than the overlying strata.

The ulcer yields an abundant purulent secretion. As it is met with almost exclusively in women suffering from syphilitic disease of the genital organs, it is probably due to infection conveyed to the rectum by the secretions escaping from the vagina. Syphilitic ulceration of the colon or small intestine is extremely rare.

477. **Intestinal mycosis** (*enteromycosis bacteritica*) is a general term, including several distinct affections. Strictly speaking it is applicable to tuberculosis, to typhoid, and perhaps to some forms of dysentery. Usually however it is confined to intestinal anthrax, and to various forms of meat-poisoning (Arts. 204, 206) by which changes in the intestine not dissimilar to those of typhoid are sometimes produced.

In intestinal anthrax we have not only diffuse and wide-spread catarrh of the bowel, but also localized changes. These take the form of small circumscribed hæmorrhagic patches, with bluish-red or brownish-red borders and a grayish or greenish yellow slough in the centre. Sometimes the patch and the slough are larger. Bacilli abound in the patches and in the surrounding tissues, especially in the blood-vessels; and also in the swollen lymphatic glands corresponding to the affected parts.

An affection of the bowel having exactly the same microscopic appearance is met with in septicæmic affections. In the case of a patient with disease of the spinal cord, who died of blood-poisoning from gangrenous balanitis and cystitis, the author found the large and small intestines beset with a multitude of small hæmorrhagic patches, each with its central slough as above described.

478. **Tumors of the intestine.** The tumor-like inflammatory growths, papillary or polypous in form, have been referred to in Art. 470. Non-inflammatory polypi of the same type are also met with, both congenital and acquired. They closely imitate the normal mucous membrane in structure, though their glands are often more abundant and at the same time more branched and convoluted. These growths are known as glandular hyperplasias, and innocent or **non-malignant adenomata.** They are rare in the small intestine, but common enough in the rectum. When pressed or dragged upon the pedicle may become

so elongated that the polypus protrudes from the anus. Individual glands are sometimes occluded and distended, giving rise to small cysts within the growth.

Carcinoma is by far the most important of the neoplasms affecting the intestine. It is not very rare as an intestinal disease, though rarer than carcinoma of the stomach. The rectum, the sigmoid, splenic, and hepatic flexures of the colon, and the cæcum, are the commonest seats. Rectal cancer sometimes extends only to the parts about the anus, but in other cases it invades the pelvic and abdominal viscera.

Carcinóma of the small intestine is rare, but in the duodenum and especially in the neighborhood of the opening of the bile-duct it is somewhat more frequent.

Intestinal cancer takes the form of soft fungous tumors which are solitary and sharply circumscribed, or of papillary roughnesses and excrescences covering a considerable area. Infiltration of the intestinal wall with cancer-cells usually takes place at an early stage, and leads to thickening and induration. If this extends round the whole circumference of the bowel, it is transformed into a thick-walled rigid tube; the rectum is the commonest seat of this indurative change, and less frequently the colon.

In most post-mortem examinations of cases of this disease we find the surface of the neoplasm already broken down, leaving a cancerous ulcer with characteristically infiltrated borders. But sometimes the borders likewise are disintegrated and eroded, and then the ulcer has quite the appearance of an ordinary non-malignant inflammatory ulcer. In other cases the borders and floor of the ulcer become scarred over and shrunken, leading sometimes to extreme constriction of the bowel: this is particularly apt to occur when the ulceration extends in an annular form round the intestine.

Carcinomata of the intestine are of various histological types. One of the commonest is the so-called destructive adenoma or **adenocarcinoma** (Art. 169). It gives rise to fungous and papillary outgrowths from the mucous membrane, and speedily invades the submucous, muscular, and serous coats. The smaller tumors consist essentially of epithelial growths resembling tubular glands and clothed with cylindrical epithelium. At later stages the glandular type in part disappears, and large solid cell-nests are formed, with cylindrical epithelial cells are at the periphery only.

Colloid carcinoma is the next in order of frequency, especially in the rectum. It takes the form of large gelatinous growths, covering a great extent of surface and infiltrating the intestinal wall. Simple carcinoma and scirrhus are rarer than either of the two just mentioned. Melano-carcinoma occurs almost exclusively in the rectum.

When a cancer of the intestine breaks down and ulcerates, at the same time invading the deeper layers of the wall, it generally induces

inflammatory changes in the serous coat. These lead to the formation of new vascular fibrous tissue, by which the affected part of the bowel is bound down to the structures around it. Perforation of the intestine occurs in some cases as a result of cancerous ulceration. Metastatic growths are usually met with, chiefly in the lymphatic glands, peritoneum, and liver.

Connective-tissue growths are rare in the intestine, and have much less significance than the carcinomata. Fibroma, lipoma, myoma, angioma, and sarcoma, have been observed.

These are developed from the mucosa and submucosa, and in part from the muscular and serous coats. When they protrude as polypi from the inner surface of the bowel they may obstruct the passage, or by their weight drag down and invaginate a portion of the wall. Pedunculated growths may be dragged upon and actually torn off by the peristaltic action of the bowel, and so be ejected with the fæces.

479. **Parasites** and **concretions.** The vegetable and animal parasites which infest the intestine have been described in detail in the General Pathological Anatomy (Arts. 182–250.)

Among the **vegetable parasites** the Schizomycetes or Bacteria are undoubtedly the most important. The bowel perpetually harbors a multitude of these fungi, of very various kinds. Hence it is difficult to say how far the various intestinal affections, and especially the inflammations, are due to the ordinary microparasites present in the fæces, and how far to distinct and specific forms. As we have indicated in the foregoing Articles, typhoid fever, tuberculosis, anthrax, and perhaps cholera and acute dysentery, are due to specific bacteria.

The Schizomycetes (Art. 183) met with in the intestine belong to the classes of Sphærobateria (*Micrococci*), Microbacteria (*Bacterium termo*), and Desmobacteria (*Bacilli, Clostridium*). In rare cases the thrush-fungus attacks the mucous membrane, but in the intestine the conditions necessary for its development seldom occur.

Of **animal parasites** the following may be enumerated. They are described in the Articles referred to.

Cercomonas intestinalis, Paramæcium coli (Art. 250).
Tænia mediocanellata or *saginata* (Art. 244).
Tænia solium (Art. 241).
Tænia nana, Tænia cucumerina (Art. 244).
Bothriocephalus latus (Art. 249).
Ascaris lumbricoides, Ascaris mystax (Art. 228).
Trichina spiralis (Art. 232).
Trichocephalus dispar (Art. 230).
Oxyuris vermicularis (Art. 229).
Anchylostoma duodenale or *Dochmius duodenalis* (Art. 231).

Of loose or foreign bodies met with in the intestine, the only ones

which have any pathological interest are those which are produced *in*

To say nothing of the hardened scybalous masses produced by retention of fæces, there are certain stony concretions which have received the name of **enteroliths,** or **intestinal calculi.** They are found chiefly in the cæcum, vermiform appendage, and colon, and more rarely in the small intestine; they usually lie in sacculations or diverticula of the wall. Three varieties have been distinguished (LEICHTENSTERN, *Ziemssen's Cyclop.* VII.).

(1) Heavy stony stratified concretions, the successive layers being white, yellow, and brown. These consist of magnesium phosphate, ammonio-magnesium phosphate, and organic matters. They are seldom larger than a chestnut, and are generally rounded in shape. They frequently contain some small foreign body as a nucleus.

(2) Enteroliths of low specific gravity and irregular form, porous and somewhat elastic in texture. They consist of a felted mass of indigestible husks and other vegetable refuse, intermingled with indurated fæces and earthy or chalky matters. They vary in size from that of a chestnut to that of an orange.

(3) Stones due to the long-continued use of certain mineral drugs, such as chalk, magnesia, and oxide of bismuth.

In addition to these, which are formed in the intestine itself, we find **gall-stones** which have escaped from the bile-duct (Art. 508).

Such concretions, and foreign bodies reaching the intestine from the exterior, may give rise to partial or complete obstruction of the bowel. Bodies lodging in the pouches of the rectum frequently do so. The result is of course stoppage of the fæces; and with this sometimes inflammation, ulceration, and perforation of the intestinal wall.

NOTHNAGEL (*Zeitschr. f. klin. Med.* III.) found that fæces frequently contain a peculiar kind of monad. When dead the organisms appear as round sharp-contoured spherules, with little refracting power. When alive they are pear-shaped, with an actively-moving flagellum at the pointed end. They change their form somewhat rapidly. In all probability they are quite harmless.

On enteroliths and intestinal concretions of all kinds see LEICHTENSTERN (*Ziemssen's Cyclopædia* VII.). In horses and horned cattle these are met with far more frequently than in human beings. The intestine of these animals always contains fragments of vegetable refuse and hairs which have been licked off and swallowed, and such matters form a nucleus for concretions to grow about. The true calculi, met with chiefly in horses, are hard stony balls consisting for the most part of magnesium phosphate. The spongy or false stones consist of felted hairs and fibres which are merely crusted over. Balls are sometimes found composed entirely or almost entirely of hairs; these go under the name of hair balls or **bezoars** or ægagropili (from αἰξ αγριος a wild goat, πιλος felt). In ruminants they usually lie in the cæcum or colon, in swine they are more frequently found in the small intestine.

FRIEDLANDER (*Berl. med. Gesellschaft* 1882, *Lond. med. Record* 1881) recently reported the case of a joiner who was accustomed to suck shellac-varnish, and

whose intestine contained a concretion consisting almost wholly of shellac. ALEXANDER (*Liverpool Med.-chir. Journ.* 1882) removed from the intestine of a fowl-dealer a bezoar containing a felted mass of downy hairs which the man had licked from his fingers while engaged in plucking poultry.

The origin and composition of intestinal calculi and concretions have been recently studied by SCHUBERG (*Virch. Arch.* vol. 90). He asserts that the intestinal concretions of the herbivora consist chiefly of carbonates, while those of the carnivora are phosphatic. In man the composition of these stones varies with the food habitually used.

For cases see LEICHTENSTERN (*loc. cit.*); BROOKHOUSE, *Lancet* 2, 1882; FELTZ, *Bulletin Soc. clin. de Paris* 1881-82; KER, *Brit. Med. Journ.* 2, 1881.

According to BIENSTOCK (*Fortschritte d. Medicin* 1883) the fæces in health contain various forms of bacilli, of which three appear to have no effect on the contents of the intestine; while another induces the putrid decomposition of albuminoids studied by NENCKI, BRIEGER, SALKOWSKI, and BERGMANN (Art. 191), and another effects the decomposition of carbohydrates. Of the last two the former is absent in the fæces of suckling infants. Micrococci are absent or scanty in healthy fæces.

SECTION VIII.

THE LIVER AND PANCREAS.

CHAPTER LV.

PIGMENTARY INFILTRATION OF THE LIVER.

480. The **liver** is the largest gland in the body, and the due performance of its functions is of essential importance to health. Its large size brings it into anatomical relation with many and various organs, and as it is only in part shielded by the wall of the thorax it is exposed to direct injuries from without which modify its form and position, and it may be its structure and function also. Its peculiar relations to the vascular system expose it to injury from the side of the circulation, and that in a twofold manner. Noxious matters, in the first place, may be brought to it, as to other organs, by the blood of the general or systemic circulation; and, in the second, by the venous blood collected by the portal vessels from the alimentary canal and spleen.

The capillary system of the liver is remarkably elaborate and capacious. Morever, the portal blood circulates under very low pressure. The circulation within the liver is therefore very slow. One consequence is—that foreign substances suspended in the blood are very apt to be deposited in the liver (Arts. 266–268), and this is true of the arterial blood (brought by the hepatic artery) as well as of the portal blood. Pigmentation or **pigmentary infiltration** of the liver-substance is the not uncommon result.

When the blood contains any considerable quantity of disintegrated red corpuscles, or of the colored iron-compounds referred to in Art. 266, and these are in part deposited in the liver, they at first lodge in the capillaries of the interlobular connective tissue (Fig. 180 *d*) or in the peripheral or portal zone of the lobules (*e*). Presently they escape from the vessels and appear in the interlobular connective tisssue, and to some extent in the interior of the liver-cells (Art. 481). When the quantity of pigment in circulation is great the pigmentation may be so dense that the structure of the tissue is completely masked by it (*d*); the biliary capillaries, and the contours of the liver-cells at the periphery of the lobules, being no longer distinguishable.

The pigment derived from disintegrated blood-corpuscles is yellow, brown, or black, and the tint communicated to the infiltrated tissue varies accordingly. As the deposit occurs chiefly if not exclusively about the portal or interlobular vessels the pigmented patches follow th[illegible] dis-

tribution (Fig. 180), and stand out in marked contrast to the pale or unpigmented central parts of the lobules.

If the blood contains, as in leukæmia, an excess of colorless corpuscles, these are in like manner deposited in large numbers in the liver and give rise to what is called **leukæmic infiltration**. The deposits are distributed in the way just described, and are sometimes enormous in amount. The liver as a whole becomes swollen, and on section the lobules appear separated from each other by a broad zone of grayish-white. Sometimes nodular aggregations of the same kind accompany the general diffuse infiltration; and the connective tissue being thereby distended and

FIG. 180. PIGMENTARY INFILTRATION OF THE LIVER.

(*After absorption of extravasated blood: carmine staining, mounted in Canada balsam;* × 20.)

a, lobule or acinus.
b, serous covering (peritoneum).
c, portal vessels.
d, infiltrated interlobular connective tissue.
e, pigment in the lobular capillaries.
f, intralobular veins.

loosened into a sort of mesh-work, the nodules have exactly the look of lymphadenoid tissue.

Noxious as well as innocuous matters may in like manner be deposited in the liver from the blood. Of these microparasites are the most important, inasmuch as their settlement in the capillaries may give rise to inflammation and necrosis of the liver-substance (Arts. 493, 494).

Structure of the liver. To understand aright the morbid changes of the liver it is necessary to have a clear and accurate idea of its normal structure. The clue to this lies in the distribution of the blood-vessels within the organ.

The hepatic vein forms a kind of tree rising from the vena cava as a base; the terminal branches are all of nearly the same size and each is at nearly the same distance from its neighbors. To each terminal branch (Fig. 180 *f*) belongs a system of capillaries, which converge from all sides towards the branch. The system of capillaries belonging to each branch is of nearly the same extent, and is grouped about the branch like a globular fruit round the central stem. The group of capillaries corresponds to the structural unit of the liver, the lobule or acinus (Fig. 180 *a*); the terminal branch or stem is the intralobular or central vein (*f*).

The meshes of the group of lobular capillaries are occupied by liver-cells, in such a way that each cell is in relation to several capillaries, and each capillary is surrounded completely with liver-cells. When seen in section the liver-cells seem grouped in columns or series, alternating with the capillaries: these columns are sometimes spoken of as hepatic trabeculæ. Where two or more liver-cells are in contact the minute radicles of the bile-ducts take their rise. A fine groove runs along the surface of contact of each cell, and the grooves being apposed an intercellular canal is thus formed. The several canals intercommunicate and so give rise to a network of bile-capillaries. The number of lobules is very great. In the human liver they are in close contact with each other, and the lobular capillary-system of one in general communicates freely with that of its neighbor. This is however not always the case, for in many parts the lobules are separated by a space filled up with connective tissue. This interlobular connective tissue is called the 'capsule of Glisson,' and serves first of all as a connecting framework for the several lobules, and secondly as a supporting sheath for the vessels which bring blood (arterial and portal) to the lobules and carry bile away from them. The latter vessels or bile-ducts are tubes lined with cylindrical epithelium, and are connected with the intralobular bile-capillaries or intercellular bile-canals already described.

The blood-supply of the liver is twofold; there is an arterial system and a portal system of vessels. The portal vessels run between the lobules (and hence are called interlobular veins), and deliver their blood directly into the lobular capillaries. The arterial blood passes in the first instance into the capillaries which permeate the connective tissue of the capsule of Glisson (vaginal and interlobular capillaries), and thence passes with the portal blood into the lobular capillaries.

Very little connective tissue accompanies the capillaries as they pass into the lobules, and it can be made out at all only by special methods of examination. The larger lymphatics lie in the interlobular connective tissue and in the sheaths of the larger blood-vessels.

481. The liver is a secreting gland, in which chemical changes of a remarkable kind are carried out. The chief products of these are—the bile-acids (glycocholic and taurocholic), to some extent derivatives of albuminoid or proteid bodies—bile-pigments, whose source is the coloring-matter of the blood—and glycogen, elaborated from the carbohydrates which are brought to the liver. A series of interchanges are thus continually going on between the glandular substance of the liver and the blood which circulates through it. Matters of various kinds are taken up and transformed in manifold ways within the liver-cells; while some substances such as fat are simply deposited or stored in the cells, and may remain unchanged for a considerable time. As certain of the normal constituents of the blood are transformed and secreted by the

liver, so also abnormal substances circulating in the blood may be taken up from it and excreted by the same channel. In this way arsenic, antimony, lead, copper, mercury, and sodium indigosulphate, are separated from the blood and cast out of the body.

In consequence of the work thus thrown upon the liver, it not infrequently shows signs of degenerative change. This is most apparent when from any cause the physiological demands upon it become excessive. When for instance in pernicious anæmia (Art. 261) the disintegration of red blood-corpuscles is greatly increased, we have not only the accumulation of pigmentary detritus around and within the lobules (Art. 480), but also an actual infiltration of the liver-cells themselves (Fig. 181). Cases occur in which almost every cell contains yellow, brown, or orange granules of pigment containing iron, especially along the central parts of the trabeculæ where the intercellular bile-canals run. QUINCKE has shown that the liver-cells also enclose colorless

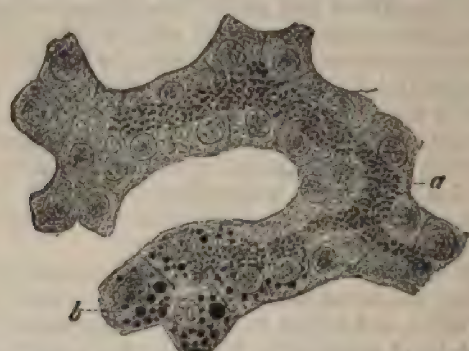


FIG. 181. LIVER-CELLS INFILTRATED WITH YELLOW PIGMENT FROM A CASE OF PERNICIOUS ANÆMIA.

(*Stained with perosmic acid and carmine:* × 350.)

a, pigment-granules.
b, cells undergoing fatty degeneration (oil-globules stained black).

granules containing iron, as may be seen by the greenish-black tint they assume when treated with ammonium sulphide. The presence of the pigment-granules is generally made apparent to the naked eye by the pale brownish-red tint they impart to the liver-substance.

The presence of these iron-compounds in the liver can be explained only by supposing that the excretion of the products of blood-disintegration through the liver cannot keep pace with the supply. The accumulation is favored by the fact that the action of the liver itself is impaired in consequence of the general anæmia. In extreme cases the liver-cells become fatty as well as pigmented, and exhibit multitudes of very minute oil-globules interspersed through their substance (Fig. 181 *b*).

The liver-cells may be affected injuriously by alterations in the composition of the blood, other than those due to its pollution with the products of its own disintegration; and the connective tissue which sheathes

and supports the vessels may likewise suffer from the same cause. Simple disturbances of the hepatic circulation, also, may of course lead to disorders of the nutrition of the liver.

Lastly, morbid changes of some danger may arise from disorders primarily affecting the biliary channels and ducts. The mere stoppage of the outflow from the common bile-duct may affect the liver seriously, and inflammation of the bile-ducts themselves are obviously still more dangerous (Art. 512).

CHAPTER LVI.

MALFORMATIONS AND MALPOSITIONS OF THE LIVER.

482. **Malformations** of the liver are not common and have little clinical importance. Absence of the organ is very rare, at least in fœtuses not otherwise gravely malformed. Abnormalities in the number of the lobes, either by excess or defect, are commoner. In a few cases accessory livers have been noted, in the form of small nodules seated in the suspensory ligament. Absence of the gall-bladder has been several times observed, as also cases of abnormal narrowness or width of the bile-ducts and abnormalities in the opening of the common duct into the intestine.

Of **congenital malpositions** the most notable are the misplacement of the liver on the left side instead of the right in *Situs transversus viscerum* (Art. 11), and protrusion of the organ into the thorax when the diaphragm is defective, or to the exterior when the abdominal wall is cleft.

Acquired deformities are very frequently the result of textural changes in the parenchyma of the organ (see under hepatitis Art. 497, syphilis Art. 499, cancer Art. 503), or of changes in the surrounding parts. Thus tight-lacing, by which the lower part of the thorax is violently compressed, gives rise to a characteristic deformity of the liver. The surface in contact with the lower ribs is indented and its fibrous capsule is white and thickened, while the liver-tissue beneath is atrophied or gone altogether (Art. 485). When the indentation is deep the right lobe is completely divided into a larger upper lobe and a smaller lower one; and in extreme cases the lower lobe becomes freely movable on the upper, and sometimes turns upwards as on a hinge.

The outer surface of the right lobe is frequently marked with shallow grooves corresponding to the ribs. The upper surface also often shows anterio-posterior grooves or furrows. According to LIEBERMEISTER these are due to wrinkles or folds into which the liver is thrown when expiration is somehow obstructed and the lower ribs dragged inwards by the abdominal muscles. ZAHN (*Rev. méd. de la Suisse romande* 1881) refers them to the pressure exerted by the hypertrophied muscular bundles of the diaphragm in cases of obstructed inspiration, and speaks of them therefore as diaphragmatic grooves. ORTH (*Pathol. Diagnostik* I.) has seen them well marked in a seven months' fœtus, and thinks they are at least in some cases congenital.

Exemption from pressure over a circumscribed area may also tend to deform the liver. This occurs for example when the diaphragm is ruptured. If the patient survives and the opening remains patent, a conical plug of liver-substance gradually protrudes into the thorax.

Displacements of the liver are very common. It turns readily on its transverse axis, so that the level of the anterior edge varies greatly with the fulness of the abdominal cavity. Actual dislocations are much rarer than such rotations; but sometimes the liver sinks abnormally owing among other things to the elongation of the suspensory ligament. This condition (*hepar mobile* or floating liver) is most marked in cases of extreme dilatation of the stomach, where the abdominal wall is at the same time much relaxed. The liver is of course forced down if the diaphragm is depressed; as in pleural effusion or pneumothorax.

Wounds and ruptures of the liver from mechanical injury are highly dangerous, and often lead to fatal hæmorrhage. Small wounds may heal in the same manner as wounds of other tissues, by the formation of granulations and a cicatrix.

CHAPTER LVII.

DISORDERS OF THE HEPATIC CIRCULATION.

483. **Anæmia** of the liver is either secondary to general anæmia, or the result of local causes. Thus pressure on the liver from without, or swelling of the liver-cells, may diminish the amount of blood present in the capillaries. The anæmic tissue is pale, and yellow or brown according to the amount of bile-pigment and of fat present in the cells. It must not be forgotten however that the distribution of the blood in the liver may be notably altered after death by the coagulation of the liver-cells and the pressure exerted on the organ by the neighboring parts; and the tint may thereby be affected in a marked degree.

Congestive hyperæmia is a very common condition of the liver, and may be either physiological (as after a meal) or pathological, as in the early stages of inflammation or in affections which determine an increased afflux of blood to the intestine. If the congestion is great the volume of the liver may be much increased, and its tissue assumes a livid or brownish-red hue.

Passive hyperæmia or **venous engorgement** of the liver gives rise to very characteristic changes, especially when it has lasted for some time.

As the liver lies very near to the right heart, every obstruction to the circulation (whether due to changes in the cardiac valves or in the lungs) which produces 'back-pressure' in the right auricle and descending vena cava, makes itself felt in the hepatic veins. The most usual causes of such obstruction are tricuspid disease, emphysema or cirrhosis of the lungs, and mitral disease.

When the engorgement is of recent standing the liver appears enlarged and full of blood, while the central parts of the lobules are dark or livid. When it is more advanced the liver usually diminishes in size, and its surface is often uneven, granular, or somewhat irregularly knobbed. On section it has a characteristic nutmeg-appearance (hence it is called '**nutmeg-liver**'), the dark centre of each lobule contrasting strongly with the pale periphery. The centre of the lobule is dark-brown and usually sinks a little below the general surface of the section while the periphery (according to the amount of fat present) is pale-brown or yellow or even yellowish-white and projects slightly above the surface. When the change has gone still further the darker portions

gradually overcome the paler, and here and there coalesce into continuous patches of brown, while the lobules generally are notably diminished in size.

On microscopic examination the intralobular veins and the neighboring capillaries are seen to be dilated or varicose; in extreme cases the dilatation affects all the capillaries of the lobule. The liver-cells which lie between the dilated capillaries are always more or less atrophied, and generally beset with yellow or brown pigment-granules. Similar granules lie around in the walls of the intralobular veins. The degeneration of the liver-cells is most marked in the central parts of the lobules, and in extreme cases some of the cells may perish outright, leaving nothing but a few granules and flakes of pigmentary detritus between the dilated capillaries. The interlobular connective tissue is usually unaltered, but now and then it appears to be hyperplastic and infiltrated with small cells.

From its chief seat and its mode of origin this affection has been described as central red atrophy (VIRCHOW), and also as cyanotic or varicose atrophy or **atrophy from engorgement.** The liver itself is described in the post-mortem room as atrophic nutmeg-liver.

484. **Occlusion of the blood-vessels** of the liver, by thrombosis, embolism, portal endophlebitis (sometimes called pylephlebitis), or endarteritis, induces certain morbid changes that are worthy of mention.

Sudden closure of the portal vein causes the secretion of bile to cease; but if the vessel is gradually obstructed and at length occluded, the secretion goes on. The nutrition of the liver itself is not endangered by the closure of the portal vein or of some of its chief branches, for the blood-supply brought by the hepatic artery suffices to maintain it in good condition.

When the portal vein or its chief branches are gradually occluded, the arterial channels gradually widen and supply the liver with blood sufficient not merely for its own nutrition but also for its functional needs. Only the obstruction of the smallest of the interlobular (portal) venules, into some of which the arterioles pour their contents before these reach the lobular capillaries, need affect seriously the corresponding lobules; and that only because the arterial circulation of the lobules is thereby at some points interrupted or diminished as well as the portal circulation, and the liver-cells being completely starved of blood perish.

The closure even of some of the branches of the hepatic artery has seldom any grave consequences, inasmuch as the branches anastomose freely and collateral circulation is readily set up. Only in somewhat rare instances, where the blood-pressure within the liver or generally through the body is low, are the propelling forces behind the point of obstruction insufficient to maintain the flow. In such a case the affected region may become engorged by reflux from the veins, and the blood escaping from the ill-nourished capillaries may give rise to **hæmorrhagic**

infiltration. Such an infiltration is however seldom so intense as to obscure altogether the outlines of the lobules. When the supply of arterial blood is entirely cut off, the liver-cells perish by necrosis (COHNHEIM and LITTEN, *Virch. Arch.* vol. 77). Hæmorrhage may likewise take place in consequence of changes in the vessel-walls (as in hæmorhagic purpura, and in phosphorus-poisoning), or of obstruction (*e.g.* by thrombosis) of the hepatic veins.

CHAPTER LVIII.

ATROPHY AND DEGENERATION OF THE LIVER.

485. **Simple atrophy.** Starvation which has been rapidly fatal, and grave chronic disorders of nutrition of long standing, may equally induce extreme atrophy of the liver. The experiments of BIDDER, SCHMIDT, and VOIT have shown that in dogs and cats starvation may reduce the volume of the liver by two-thirds. The diminution is chiefly due to the dwindling of the liver-cells. In emaciated or marasmic patients, whether the wasting is due to senile decay or to organic disease, the liver is usually greatly diminished in size, and in some cases occupies only one-third of its original volume.

The atrophy is seldom uniform, the margins of the organ being usually the most wasted. The anterior margin of the right lobe and the whole margin of the left are often very markedly shrunken. In extreme cases the parts just mentioned, as well as other regions (notably along the line of the suspensory ligament), may be altogether devoid of liver-cells.

The atrophy in these cases is primarily due to loss of the liver-cells, which become steadily smaller (Fig. 183 *A*) and at length vanish outright. The trabeculæ and lobules dwindle, and the interlobular or portal sheaths of connective tissue (Fig. 182 *d*) approach each other. When the lobules have entirely disappeared, the meshes enclosed by the portal sheaths enclose mere shreds of loose fibrous tissue (*e*) composed of little else than collapsed capillaries. The bile-ducts within the portal sheaths (*f*) persist however, and in some parts seem even increased in number; at any rate a section through the interlobular structures often shows that at certain points whole clusters and groups of bile-ducts have been cut across (*f*).

The atrophic tissue is usually poor in cells; but if any obstruction to the outflow of bile has taken place, signs of inflammation and cellular infiltration may be seen (Art. 496).

The wasted borders of the lobes may be reduced to mere membranes, and look like thickenings of the serous coat. As the right lobe shrinks the gall-bladder is uncovered, and sometimes projects far beyond the wasted border.

Where the liver-substance still persists the remaining lobules are usually small, and often abnormally brown in color. This is due to the

fact that some of the liver cells are beset with pigment-granules (Fig. 183 *A*).

486. **Pigmentary atrophy.** The atrophy just considered (Art. 485) is a general affection extending over the whole of the liver, and depending on impairment of its nutrition. Localized atrophy affecting a few cells or lobules is a very common condition, and may be induced by a great variety of causes. Thus we have seen that long-standing venous engorgement of the liver constantly leads to atrophy of the central parts

FIG. 182. SECTION FROM THE MARGIN OF A GREATLY ATROPHIED LIVER.

(*Carmine staining* : × 30.)

a, serous membrane.
b, completely atrophied region.
c, normal lobules.
d, portal sheaths enclosing blood-vessels and bile-ducts *f*.
e, loose fibrous tissue taking the place of the lost liver-substance.
f, bile-ducts.
g, larger portal veins.
h, intralobular veins.

of the lobules (Art. 483). So also where the fibrous framework of the organ becomes hypertrophied, as in indurative hepatitis (Art. 497), the liver-cells are usually compressed and atrophied. Mechanical pressure from without or within may have the like effect. The latter is observed in the neighborhood of tumors and other new-formations growing in the liver; amyloid disease (Art. 491) affords a good example. The liver-cells

are usually deformed and flattened (Fig. 183 *B*), or drawn out into long spindles.

The atrophied cells are usually beset with brown and yellow pigment-granules. These are probably due not so much to re-absorption of bile already elaborated and excreted as to some disturbance of the process of secretion itself. The ill-nourished cells are unable to perform their normal bile-producing function, and as the colored iron-compounds are no longer adequately separated and excreted, they perforce remain in the cells. In certain cases, however, the cause of the pigmentation may lie in some increase in the normal disintegration of the red corpuscles (Art. 81).

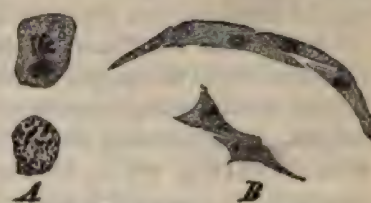


FIG. 183. ATROPHIED LIVER-CELLS (× 250).

A, simple atrophy with pigmentary deposits.

B, liver-cells atrophied by compression.

487. **Fatty infiltration.** The liver in health always contains a certain amount of fat, which lies in the liver cells in the form of large and small globules (Fig. 184 *a b c*). This fat is partly brought to the liver ready-formed and there deposited, and partly elaborated from albuminoid substances *in situ*. The former fat is either derived directly from the food, or has been elaborated from albuminoids in some other part of the body.

In morbid conditions the fat contained in the liver may be enormously increased; the increase depending either on increased production or supply, or on diminished consumption, or on both.

When fat accumulates as a deposit in the liver, from increased supply or decreased consumption, we have what is called simply **fatty liver**, or fatty infiltration. When the accumulation is great the liver is large, and *post-mortem* feels firm to the touch, holds little blood, and has a uniform opaque pale-yellow tint. The individual lobules are somewhat enlarged.

When the quantity of fat present is not so great, it lodges chiefly in the peripheral parts of the lobules. These parts consequently look pale, while the central parts are brown or reddish; and the mottled appearance thus produced has led some to describe this variety as fatty nutmeg liver. If the fat be still less abundant the general brownish color of the lobule prevails.

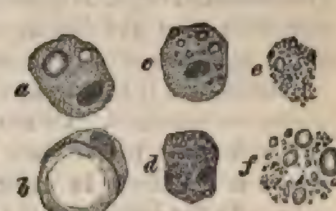


FIG. 184. FATTY LIVER-CELLS (× 400).

a, *c*, cells with several oil-globules.

b, cell with one large drop.

d, cells with many minute globules.

e, *f*, cells completely disintegrated into fatty detritus.

Fatty livers are met with most commonly in corpulent patients; but they are not rare in cases of lung-disease associated with much ema-

ciation. In the latter we must suppose that the accumulation is due to defective consumption of the fat.

The fat usually takes the form of large drops which distend the cells (Fig. 184 *b*); though at first it is deposited in smaller globules (*a c*). As the fat is re-absorbed the large drops break up again into smaller ones.

488. When the disintegration of albumen within the liver becomes excessive, while the supply of albumen is not sufficiently maintained, the process assumes a degenerative character and is described as **fatty degeneration.** In slight cases the liver-cells are more or less thickly beset with oil-globules (Fig. 181 *b*), but are otherwise little changed; where the degeneration is advanced the cells break down altogether (Fig. 184 *f*).

Simple uncomplicated fatty degeneration is well observed in extreme anæmic conditions, such as that known as pernicious anæmia. Here the process is characterized throughout by the formation of very minute oil-globules, and is often accompanied by pigmentary infiltration.

Fatty degeneration frequently sets in with **cloudy swelling** (Art. 48) of the cells, which enlarge and become turbid and granular. The liver as a whole thereupon assumes a muddy grayish or grayish-yellow tint, and sometimes looks as if boiled. This stage of the degeneration is met with in many forms of infective disease, such as typhoid, relapsing fever, small-pox, scarlatina, septicæmia, erysipelas, yellow fever, etc., and in poisoning by antimony, arsenic, sulphuric ether, and phosphorus.

In most cases the turbidity and swelling disappear and the cells recover their normal aspect. In other cases the process passes into fatty degeneration and disintegration of the affected cells. These changes are most marked in phosphorus-poisoning and in acute yellow atrophy.

489. **Acute yellow atrophy.** The affection so named is characterized by a great and sudden diminution of the size of the liver. Within a few weeks or it may be days the liver loses as much as half its bulk. The shrunken organ is remarkably flaccid and soft, and here and there may even give the feeling of fluctuation. Sometimes however it is firmer, the surface being smooth or wrinkled in different cases.

The section is usually of an ochreous yellow, and the contours of the lobules are obscured. Or the yellow tint may appear only in some spots, while others are pale or dark red (so-called 'red atrophy'). The single lobules are uniform in color, or now and then show variously tinted zones. In the latter case the periphery is grayish and semi-translucent, while the central parts are of various shades of yellow, and now and then the very centre is red. The differences in size, consistence, and color are due partly to differences in the condition of the liver-cells, partly to the amount of blood present in the vessels.

As regards the liver-cells, they are found in the most diverse stages of degeneration, from mere dropsical and cloudy swelling to complete disintegration into masses of fatty and albuminous detritus. At the

same time the cohesion of the several cells is loosened. In the ochreous parts few if any cells remain unaltered. Those that are least altered are turbid and beset with granules and oil-globules; the most altered consist of little else than drops of oil of various sizes, while many are completely broken up or in process of solution (Fig. 184 *e f*). In the grayish semi-translucent parts a few normal cells remain, but the greater number are disintegrated and replaced by irregular clumps of colorless albuminous granules, grains of yellow pigment, and small and large drops of oil. At many points even these remains of cells have disappeared and the intercapillary spaces contain nothing but liquid. The detritus has been partly dissolved and partly removed by the lymphatics.

The amount of blood present in the vessels varies much: when present it gives to some parts the red tint to which we have alluded. What is called 'acute red atrophy' is in fact 'yellow atrophy' associated with a more than usually abundant supply of blood to the parts. Naturally the red appearance becomes more appreciable as the fatty detritus of the disintegrated tissue is dissolved away or otherwise removed. The brown or darker yellow tints are due to pigment-granules which lie in the tissues that remain.

In the later stages of the affection the periportal connective tissue is slightly infiltrated with lymphoid cells or leucocytes; in the earlier stages these are absent. When the process is still more advanced leucin and tyrosin accompany the oily deposits, or at least become apparent some hours after death.

490. Acute yellow atrophy is thus characterized texturally by a fatty degeneration of the liver depending on a rapid disintegration of the albuminoid constituents of the liver-cells. The ætiology of the process is not always the same. In a few cases it is an accompaniment of recognized infective disorders, especially of traumatic septicæmia. In other cases its causes are unknown, and then it would seem to be an idiopathic or at least a primary affection. Probably in these cases also it is due to some kind of microparasitic infection. In support of this view it is to be noted that KLEBS has on several occasions discovered micrococci crowding the hepatic vessels in cases of acute yellow atrophy unaccounted for by the presence of any other source of infection.

But apart from causes of the nature of infection, it is known that certain poisons, notably phosphorus, may give rise to degenerative changes closely resembling those we have just described. In **phosphorus-poisoning** we may have various degrees of change, from mere turbidity of some of the liver-cells and the formation of a few oil-globules to extreme and extensive fatty disintegration of the liver-substance generally. In a few days after a poisonous dose of phosphorus has been taken the greater part of the liver may be broken down into fatty detritus. The changes begin in from six to twenty-four hours, and first appear round the periphery of the lobules. The cells become turbid and swollen, then

oil-globules appear which as a rule soon run together into larger drops as the cell disintegrates.

The color of the liver in phosphorus-poisoning is grayish-yellow or yellow, and the organ feels greasy and doughy. In the early stages, that is before the liver-cells are entirely disintegrated and before their remains are absorbed, the liver is enlarged. Sometimes small hæmorrhages take place into the tissue. When these are confined to the portal areas peculiar rosette-like figures are produced by the extravasated blood. Now and then the liver looks as if bile-stained. As the degeneration advances the secretion of bile is more or less interfered with. In the later stages leucin and tyrosin are deposited, as in acute yellow atrophy.

After a time the tissue of the atrophied liver is seen to contain clusters and more and less cylindrical groups of large epithelial cells. These are considered to be gland-cells, and to indicate the beginning of a process of regeneration and repair. Some observers regard them as derived from the epithelium of the bile-ducts, others from the surviving liver-cells. The author's observations incline him to support the latter view; he believes that the surviving liver-cells may have the power to multiply and build up new liver-tissue. The longitudinal groups or cylinders sometimes include large cells with abundant protoplasm and very large nuclei (occasionally of double the normal size); and these at least would appear to be proliferous cells.

COHNHEIM (*Allg. Path.* II. Berlin 1882) and others distinguish the affection known as *icterus gravis* or **malignant jaundice** from acute yellow atrophy of the liver. The former is marked by complete suppression of the biliary secretion and by intense jaundice; both of these systoms may be absent in typical cases of the latter.

References on acute yellow atrophy: FRERICHS, *Diseases of the liver* II. (trans. by MURCHISON, New Syd. Soc.) London 1862; KLEBS, *Handb. d. path. Anat.* I. Berlin 1869; ZENKER, *Deutsch. Arch. f. klin. Med.* X. (1872); VON WINIWARTER, *Wiener med. Jahrb.* 1872, LEWITZKY and BRODOWSKY, *Virch. Arch.* vol. 70; AFFANASIEW, *Pflüger's Archiv* XXX.; MOXON, *Trans. Path. Soc.* XXIII. (1872); THIERFELDER, *Atlas d. path. Hist.* part 3, 1874, *Ziemssen's Cyclop.* IX., with full references; MURCHISON, *Diseases of the liver* London 1877; BIRCH-HIRSCHFELD, *Gerhardt's Handb. d. Kinderkr.* IV. Tübingen 1880; ZUNDER, *Virch. Arch.* vol. 59; LEGG, *Bilious Diseases* London 1880, with a very complete summary of the literature; HLAVA, *Prager med. Woch.* 1882; SALKOWSKI, *Virch. Arch.* vol. 88; NOMAN, *ibid.* vol. 91; GOODHART, *Atlas of Path.* (New Syd. Soc.) London 1883.

On the micro-organisms associated with the affection see WALDEYER (*Virch. Arch.* vol. 43), KLEBS and EPPINGER (*Prager Vierteljahrsschrift* 125, 1875), DRESCHFELD (*Brit. med. Journ.* 2, 1883).

On the liver in phosphorus-poisoning see LEYDEN and MUNK (*Die acute Phosphorvergiftung* Berlin 1865), KLEBS (*loc. cit.*), WEYL (*Arch. d. Heilk.* XIX.), LEBERT and WYSS (*Arch. gén. de méd.* 1868), SCHULTZEN and REISS (*Charité-Annalen* 1869), FRAENKEL (*Berl. klin. Woch.* 19, 1878), ERMAN (*Viertelj. f. gericht. Med.* XXXIII.), BINZ and SCHULZ (*Cent. f. d. med. Wiss.* 1879), CORNIL and BRAULT (*Journ. de l'anat. et de la phsiol.* 1882), WEGNER (*Virch. Arch.* vol. 59), VOIT and BAUER (*Journ. Chimical Soc.* XXIV.), LEGG (*Bilious diseases* London 1880),

OSSIKOVSZKY (*Wien. med. Wochenschrift* 31, 1881), THIERFELDER and NAUNYN (*Ziemssen's Cyclop.* IX., XVII., with references), TAYLOR (*Medical Jurisprudence* I. London 1883).

491. **Amyloid degeneration.** Amyloid change affects chiefly the lobular systems of blood-vessels. At first the capillaries of the lobules exhibit at various spots a kind of hyaline thickening or deposit in the endothelium; but as the change progresses they become completely enveloped by continuous hyaline masses (Fig. 185).

The liver-cells are usually passive throughout the process, or at least they rarely become amyloid themselves. In the early stages they are quite unaltered, but as the amyloid deposits around them increase in bulk they become compressed and generally atrophied. In advanced stages they here and there perish outright, or it may be that to some extent amyloid deposits take place in them. Where they persist they nearly always contain large or small globules of fat.

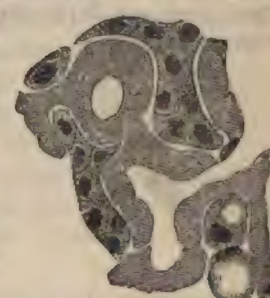


FIG. 185.—AMYLOID LOBULAR CAPILLARIES.
(*Treated with perosmic acid:* × 300.)

Amyloid change also, though to a less degree, affects the interlobular blood-vessels. In the case of the arteries the middle coat is the most affected.

The change usually extends over the whole of the liver, and when it is well-marked the section becomes pale grayish-brown or grayish-yellow in color, and it has a semi-translucent appearance like the fat of boiled bacon. The semi-translucent patches are chiefly found in the intermediate zone of the lobule, the neighborhood of the central or intralobular vein on the one hand and of the portal vein on the other being comparatively free from deposit. In other instances however there seems to be no special arrangement of the amyloid patches. Iodine gives the characteristic brown color, and methyl-aniline a pale ruby tint (Art. 58).

The unaltered tissue varies in appearance in different cases. When the liver-cells contain no fat, they are usually of a brown or reddish-brown color. The presence of fat makes them look yellowish-white.

Well-marked amyloid change is always associated with enlargement of the liver. The edges are thickened and rounded and the surface is smooth, but the serous covering is free from thickening. The tissue becomes firmer and much more elastic. The amount of blood contained in it varies but is generally small, at least in the more degenerate portions.

General amyloid disease of the liver occurs chiefly in connection with cachectic conditions, such as those depending on tuberculosis, chronic suppuration, syphilis, etc. Other organs are simultaneously affected in a similar manner, especially the spleen, intestine, and kidneys.

The liver may at the same time be diseased in other ways; thus in

tuberculosis it may contain tubercles, and in syphilis it may exhibit the characteristic hyperplasia of the periportal connective tissue (Art. 499) or gummatous foci in various stages.

Circumscribed amyloid change of the liver, limited to one or more spots, is much less common than the uniformly diffused or general affection; but it is occasionally met with. Cases are recorded in which the amyloid substance was aggregated into nodes or nodules, or confined to a few isolated blood-vessels. The latter is especially the case in the vessels of cicatricial tissue developed in consequence of syphilitic inflammation.

References:—Arts. 58, 59; WILKS, *Guy's Hosp. Rep.* 1856; WAGNER, *Arch. d. Heilk.* II. (1861); CORNIL, *Arch. de physiol. norm. et path.* II. (1875); HESCHL, *Wiener Sitzungsber.* LXXIV. (1876); SCHÜPPEL, *Ziemssen's Cyclop.* IX.; BÖTTCHER, *Virch. Arch.* vol. 72; SCHÜTTE, *Die amyloide Degen. d. Leber* In. Diss. Bonn 1877, with good figures.

CHAPTER LIX.

HYPERTROPHY AND REGENERATION OF LIVER-TISSUE.

492. When from any cause the glandular cells of the liver are destroyed, as in phosphorus-poisoning, the tissue may to a certain extent be repaired or renewed by regenerative multiplication of the remaining cells. How far the process of regeneration can go we do not as yet fully know; but we may well suppose that it is possible only when the loss of substance is small and the general structure of the lobule not gravely damaged. We suggested in Art. 490 that the process of regeneration starts from the liver-cells within the injured lobule, and it certainly seems highly improbable that an entire lobule or any part of one should be developed from the epithelium of the biliary ducts.

As to the histology of hypertrophy of the liver-tissue there is but little to say.

Enlargement of the liver is chiefly due to deposits of fat or of amyloid substance, to new-formed fibrous tissue, or to infiltration with leucocytes (as in leukæmia). In a few cases the enlargement of the liver has been found to be congenital, the structure being normal. Ricketty children not infrequently have remarkably large livers (BENEKE). And in adults abnormal size of the liver is now and then discovered, without any assignable cause for the enlargement. Inasmuch as the volume of the organ may vary in health within somewhat wide limits, it is difficult to say at what point an enlargement is to be regarded as morbid. The statement sometimes made—that the liver in diabetes is apt to be very much enlarged—cannot be corroborated by the author.

The lobules of an abnormally large liver are not usually enlarged, and hence one must assume that their number is increased. As regards the size of the liver-cells, it is known that this varies under physiological conditions; it is therefore difficult or impossible to detect what we may call cellular hypertrophy, if it exists. Sometimes when one part of the liver-substance perishes the remainder seems to enlarge; but on closer examination the local hypertrophy is seen to be more apparent than real, the appearance being mainly due to contraction, compression, and displacement of the several parts.

Circumscribed hypertrophies or hyperplasias of the liver-tissue do however occur in the form of nodules or larger nodes (FRIEDREICH, *Virch. Arch.* vol. 33; HOFFMANN, *ibid.* vol. 39; EBERTH, *ibid.* vol. 43).

These protuberant overgrowths consist of liver-tissue, the cells of which are abnormally large and arranged in somewhat irregular groups or trabeculæ.

References: TIZZONI, *Atti della r. acad. dei Lincei* 1883, *Arch. ital. de biol.* III. (1883); COLUCCI, *ibid.*, *Studj sull' anat. patol. d. fegato* Bologna 1883. These authors assert that in the lower animals at least wounds of the liver are partly repaired by new-formations of liver-tissue, and that these new formations may reach a considerable size.

CHAPTER LX.

INFLAMMATIONS OF THE LIVER.

Purulent hepatitis and Hepatic abscess.

493. **Purulent inflammation of the liver** depends on the invasion of the organ by some noxious or irritant body derived either from the exterior or from some other part of the system.

The information we now possess concerning the genesis of the suppurative process justifies us in believing that as a rule this irritant is a bacterium or is produced by the agency of bacteria. Only in very peculiar and unlikely conditions can any other agent (such as the *Actinomyces*) give rise to suppuration within the liver.

The avenues by which micro-organisms may enter the liver are numerous. They may enter directly from without in the case of a perforating wound of the liver through the belly-wall, and cause the wound to suppurate. A purulent inflammation of any of the neighboring organs or tissues may extend to the liver by continuity, or through the channel of the lymphatics. More commonly however the micro-organisms reach the liver through the blood. The portal vein is the most frequent channel, though the hepatic artery may also convey infection. Rarely, and only in very exceptional circumstances, can anything of the kind pass with the venous blood from the vena cava into the hepatic veins. Lastly, in infants the patent umbilical vein may convey infection to the liver.

Infection of the liver by these channels is commonly secondary; that is, it depends upon a preceding lodgment of bacteria somewhere within the territory supplied by the blood-vessels in question. Thus abscess of the liver is not infrequently the result of purulent inflammation (dysentery) of the intestine, infection being conveyed by the portal vein; or it may follow upon a suppurating wound of the head for example, the channel of infection being the hepatic artery. In the latter case the virulent material must have passed through the lungs, and may there also give rise to secondary suppuration.

Primary suppuration within the liver, that is to say suppuration unaccounted for by the existence of some focus of infection elsewhere in the body, is rare in temperate climates. In the torrid zone hepatic abscess ('**tropical abscess**') is a very common affection, and it is frequently impossible to detect a source of infection in any other organ or

part. In a large number of cases however the hepatic abscess is preceded by dysenteric disease of the bowel.

There is still another avenue by which an irritant capable of exciting inflammation may reach the liver, namely the common bile-duct. When the biliary channels are somehow diseased so that bile is retained and stagnates within them, concretions may be formed, and these appear to favor the entrance of noxious matters into the liver.

494. When a bacterium (such as the micrococcus of pyæmia, Art. 204) capable of giving rise to inflammatory change enters the liver through the blood, it lodges first in the capillaries (Figs. 186, 187 c) and afterwards in the smaller venules. Then it forms colonies or zooglœa, which presently fill up and it may be distend the vessels. After a short time the liver-cells become turbid and swollen, they lose their nuclei, and soon break up into fragments of various sizes (Fig. 186).

FIG. 186. *MICROCOCCUS SEPTICUS* IN HEPATIC CAPILLARIES.
(*Forming zooglœa: aniline-brown staining:* × 350.)

As the colonies multiply they spread more and more widely through the vessels, so that soon a great number of affected lobules have their capillaries (Fig. 187 c), and often their intralobular veins (c e), crammed with bacteria. The necrosis of the liver-cells (b) advances steadily with the advance of the invasion.

These changes are accompanied by intense inflammation of the interlobular tissue (d) and the veins (e), which gives rise to an abundant cellular infiltration of the tissue around. This is the first stage in the formation of an abscess. Soon the infiltration of cells and exuded liquid becomes more marked, and the necrotic cells break up and liquefy. A collection of pus is thus produced, and a **hepatic abscess** is formed.

This is in brief the course of the process; but of course it may be modified in numerous ways. Thus the micrococci may settle in the connective tissues, or a number of lobules may be simultaneously affected and break down, and so on. Abscesses starting in wounds or in the bile-ducts (Art. 512) will naturally exhibit peculiarities of their own. In the latter case, for instance, the irritant matters will first affect the walls of the ducts and their surroundings, and set up inflammation there.

495. The appearance presented by a hepatic abscess varies with its mode of origin and its age.

When infection is conveyed by the blood-vessels the affected lobules look gray or grayish-yellow. Then the parts that are on the point of suppurating become yellow or yellowish-white, and presently the whole of the affected patch breaks down into dirty yellowish pus, either liquid throughout or mingled with discolored shreds of necrotic tissue. The

surrounding parts are discolored, infiltrated with pus, and in process of liquefaction. The abscesses may be single or multiple. The remaining parts of the liver show a greater or less degree of turbid swelling, sometimes accompanied by extravasations of blood which become slaty-gray in color when putrefaction sets in.

In abscess from a suppurating wound of the liver some traces of the original injury are usually to be seen. In biliary abscess (if we may so

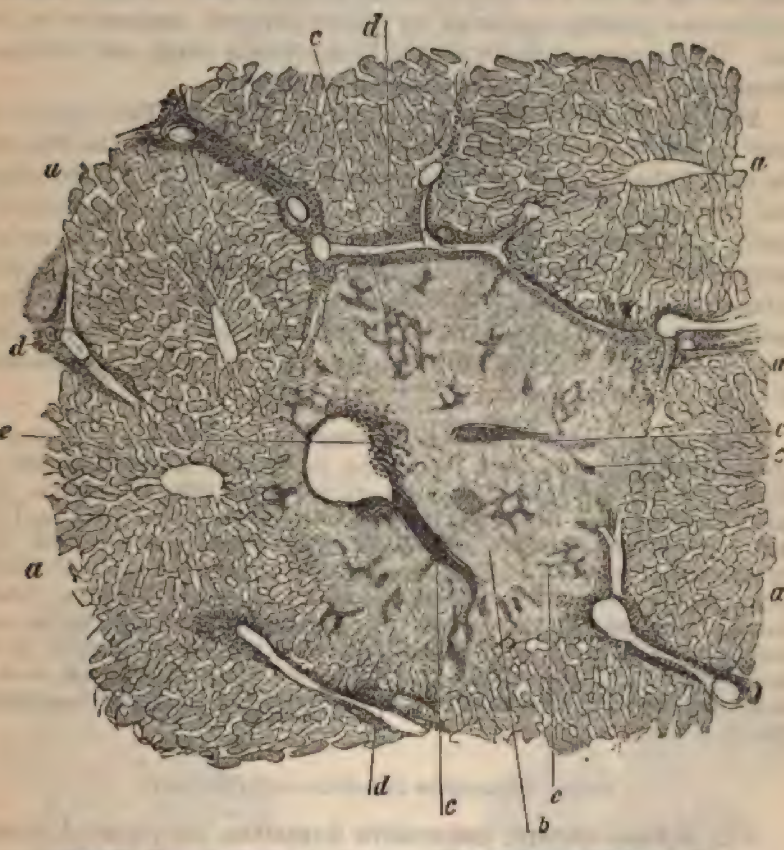


FIG. 187. HEPATIC ABSCESS: FIRST STAGE. (*Bismark-brown staining*: × 40.)

a, normal lobules.
b, necrosed lobules.
c, capillaries and venules filled with micrococci.
d, small-celled infiltration of the interlobular tissue.
e, aggregation of small-round cells in a vein, into which opens an intralobular venule crammed with micrococci.

describe it) the pus is mingled with bile or with biliary concretions. When the abscess lies immediately beneath the serous membrane the latter is more or less intensely inflamed.

The size of hepatic abscesses varies; it may extend to almost an en-

tire lobe. Minute multiple abscesses sometimes coalesce into larger ones.

In very many cases abscess of the liver, or the injury to which it is secondary, brings about the death of the patient. But when death does not take place, granulation-tissue is developed around the abscess-cavity and forms for the rest of the tissue a kind of protecting membrane. Small abscesses may disappear, their contents being entirely absorbed; and a scar varying in size with the size of the abscess is left. Larger abscesses may become notably contracted by absorption and inspissation of the pus. The inspissated pus is always enclosed by a tough and thickened fibrous wall, and sometimes becomes calcified.

Abscesses frequently break into surrounding parts. This issue is the most favorable when adhesions have been set up between the liver and the wall of the abdomen or of the intestine, and the pus is then evacuated through the adherent parts to the outside of the body or into the bowel. Even rupture through the diaphragm into a bronchus is not entirely unfavorable; but rupture into the cavity of the pleura, pericardium, or peritoneum, is highly dangerous. General inflammation of the corresponding serous membrane is the result, unless the previous adhesions between the liver and other viscera are such as to limit the extension of the inflammatory process.

References:—FRERICHS, *Klinik d. Leberkrankheiten*, *Diseases of the liver* II. London 1862; VIRCHOW, *Virch. Arch.* vol. 4; TRAUBE, *Gesam. Abhandl.* II.; ROUIS, *Rech. sur les suppurations endém. du foie* Paris 1860; BAMBERGER, *Virchow's Handb. d. spec. Path.* 1864; BÜCKLING, 36 *Fälle v. Leberabscess* In. Diss. Berlin 1868; KLEBS, *Handb. d. Path. Anat.* II.; ACKERMANN, *Virch. Arch.* vol. 45; HEINEMANN, *ibid.* vol. 58; THIERFELDER, *Atlas d. path. Hist.* plate XV. *Ziemssen's Cyclop.* IX., with full references to the older papers; MCCONNELL, *Indian annals of med. sci.* 1873; many papers by MURCHISON, BRISTOWE, QUAIN, and others in the earlier vols. of the *Trans. Path. Soc.*; MURCHISON, *Diseases of the liver* London 1877; LEBERT, *Arch. f. klin. Med.* VI.; BIRCH-HIRSCHFELD, *Arch. f. Heilk.* XIV.; HIRSCH, *Handb. d. histor.-geog. Path.* II. (trans. by CREIGHTON, New. Syd. Soc.).

Chronic indurative hepatitis and Cirrhosis.

496. **Diffuse chronic indurative hepatitis,** like purulent hepatitis, depends on noxious influences which reach the liver by various channels. Of these channels the blood-vessels are the chief, though the bile-ducts also are very often at fault; in other words the disease is most frequently hæmatogenous, though instances of what we may call biliary hepatitis are by no means uncommon. As to the exact nature of the noxious influences or agents we know little. It is possible that in many or in most cases irritant matters absorbed from the alimentary canal are especially concerned. By many authorities alcohol is considered to be one of the most important of the exciting factors. In other cases syphilis is admittedly the cause.

Indurative inflammation of the liver is always a chronic and at the same time a very gradual and insidious affection. It is rare for an acute hepatitis to pass into a chronic one of this type.

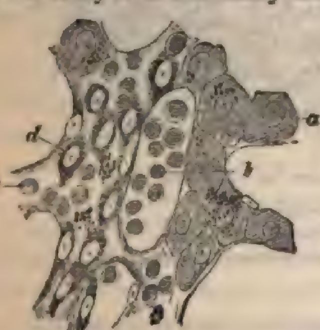
The first stages of the affection are marked by the presence of a more or less obvious infiltration of the liver-tissue with leucocytes.

FIG. 188. RECENT INTERSTITIAL HEPATITIS.

(*Hæmatoxylin staining:* × 80.)

a, normal liver-tissue.
b interlobular connective tissue infiltrated with leucocytes.

The infiltration is chiefly seen in the interlobular connective tissue (Fig. 188 *b*), and thence extends into the lobules. The infiltration is usually at first in the form of disconnected patches of various sizes. Less commonly it is uniformly diffused.



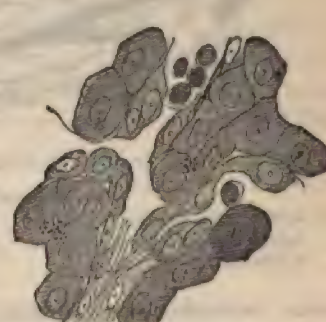


FIG. 189. EXTRAVASCULAR DEVELOPMENT OF NEW FIBROUS TISSUE IN THE LIVER.

(*Carmine staining:* × 300.)

a, normal liver-cells.
b, accumulation of leucocytes within a capillary.
c, leucocytes in the place of the liver-cells.
d, formative cells or fibroblasts.

FIG. 190. INTRAVASCULAR DEVELOPMENT OF NEW FIBROUS TISSUE IN THE LIVER.
Fibroblasts and small leucocytes are seen lying within the capillaries.

From the extravasated cells new fibrous tissue is gradually elaborated by the development of fibroblasts, that is to say of large cells with clear

vesicular nuclei (Fig. 189 *d*). When the process extends to the lobules leucocytes accumulate within the lobular capillaries (Fig. 189 *b* and Fig. 190), and from them are developed fibroblasts (Fig. 190) and ultimately fibrous tissue.

The growth of fibrous tissue may be extravascular as well as intravascular, leucocytes and fibroblasts appearing between and among the liver-cells (Fig. 189 *c*) and presently compressing or displacing them. A certain number of the liver-cells consequently become atrophied and per-

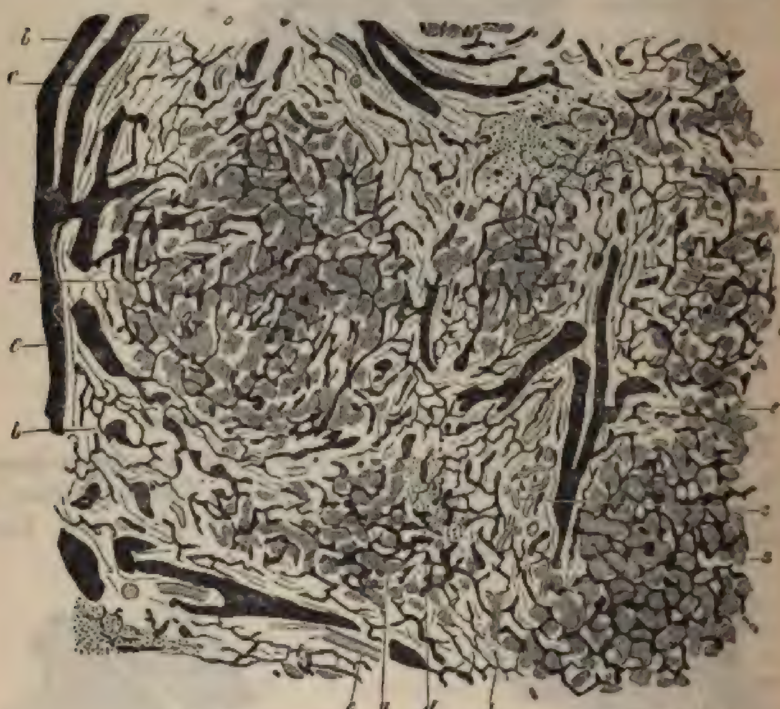


FIG. 191. GRANULAR ATROPHIC CIRRHOSIS OF THE LIVER.

(*Arteries injected; carmine staining;* × 25.)

a, remains of normal lobule.
b, new-formed fibrous tissue.
c, bile-ducts.
d, infiltration of leucocytes.
e, interlobular (portal) veins.

ish. In some cases this atrophy by compression is very considerable, in other cases the cells persist in a remarkable way.

As a result of the destruction of liver-cells, which perish by fatty degeneration as well as by simple atrophy, deposits of yellow and brown pigment appear in the affected tissue. Part of this is derived from the coloring-matter of the blood, in consequence of the interference with the secretion of bile; part is probably derived from bile actually secreted, but retained in consequence of the blocking of the bile-channels. The new-formed fibrous tissue is frequently infiltrated with bile-pigment.

The bile-ducts are seldom greatly obstructed, or diminished either in size or number. Indeed in some forms of hepatitis they appear to be multiplied.

497. When indurative hepatitis has lasted for some weeks or months the connective tissues of the liver always exhibit a more or less marked hyperplasia.

This is chiefly shown in the fibrous portal sheaths (Fig. 191 *b*) which appear broadened and thickened. In some cases the fibrous overgrowth is almost entirely confined to the interlobular structures; but it often extends to the lobules, creeping along the lobular capillaries and intruding itself between the columns of liver-cells (*a*). In this way many groups of liver-cells become surrounded, and appear in the midst of the overgrown fibrous tissue; they are thus more or less separated and cut off from their capillaries. The result is that some of them perish, while others which survive give rise to clusters and strings of cells looking very like bile-ducts; these have indeed been regarded by some as new-formed bile-ducts. This view is certainly not correct, though the strings of cells do in fact act as channels for the bile between the isolated remnants of liver-tissue and the true bile-ducts. The latter are unaffected by the other changes in the organ and in some cases may actually be increased in number. ACKERMANN succeeded in injecting the new-formed channels from the hepatic duct. It is however to be noted that the multiplication is often only apparent. The ducts which enter the lobules, and they do so to a greater depth than the descriptions in the histological text-books would imply, are normally concealed by the overlying liver-cells; and as these latter shrink or disappear the ducts become much more distincty visible.

The hyperplastic connective tissue when fully developed is dense and fibrous; it usually contains but few cells, though in parts the extravasated cells still remain (Fig. 191 *d* and Fig. 192 *c*) as evidence of the inflammatory infiltration. Sometimes indeed they are so abundant that the new fibrous tissue looks as if it were itself infiltrated.

The interlobular fibrous tissue is usually highly vascular. A certain portion of the portal vascular system is obstructed or obliterated by the inflammatory changes in the smaller vessels, but some of the interlobular veins always remain patent (Fig. 191 *e*).

As the portal capillaries are obliterated the circulation in the portal vein becomes obstructed. This leads to **portal engorgement,** to swelling of the spleen, to ascites, and frequently to hæmorrhage. The lobular circulation is however not entirely interrupted, for the hepatic artery partly takes on the functions of the portal vein. The main branches dilate, the smaller branches increase in number, and furnish blood to the thickened and overgrown capsule of Glisson as well as to the lobules. But it must be kept in mind that, in the varieties of hepatitis in which the liver becomes contracted, this blood-supply is manifestly insufficient

for the nutrition of all the liver-cells. The result is that the cells sometimes very rapidly undergo fatty and pigmentary degeneration and actual necrosis.

The gradual obstruction of the portal circulation within the liver leads to the opening up of the vascular connections between the tributaries of the portal vein and the veins of the abdominal wall, the diaphragm, the œsophagus, and the capsule of the kidney, the lumbar veins, and the spermatic veins. Now and then the subserous veins of the round (umbilical) ligament become dilated and continuous with the subcutaneous veins around the umbilicus, and so give rise to a tortuous plexus of dilated veins visible on the surface and known as a *caput medusæ*.

498. The extent of the inflammatory change depends in the first place on the mode of diffusion of the irritant through the liver. Inflammation starting from the portal vessels and inflammation starting from the hepatic artery differ notably in this respect. The inflammatory change may be limited to one or more branches of the respective vessels, or it may extend uniformly over the territory supplied by one or by the other. In the former cases the affected parts are scattered and isolated; in the latter the interlobular tissue throughout the liver is uniformly affected and altered. As the change extends from the interlobular tissue to the lobules and approaches the region of the intralobular vein, it of course tends to become more and more uniform and diffuse. Between the extremes of a few isolated patches and an alteration of the liver-tissue which is uniformly diffused there may be any number of intermediate grades.

The variety of inflammation which starts in the bile-ducts, or so-called **biliary hepatitis**, has certain peculiarities. It generally arises in connection with retention of bile, and engorgement of the biliary canals (Art. 512). The inflammation is at first confined to circumscribed patches, usually round in shape and infiltrated with bile-pigment. The patches lie either in the interlobular tissue or within the lobules. The inflammation is sometimes of the plastic or formative type and sometimes purulent.

Recent inflammation of the liver is always accompanied by swelling of the whole organ, which is more marked as the inflammation is more extensive. Minute patches of inflamed tissue may not be recognizable by the unaided eye, but when they reach any perceptible size they appear gray or grayish-red.

When fibrous tissue is developed in consequence of antecedent inflammation the enlargement of the liver becomes still more marked. This secondary enlargement is naturally greatest in cases where the affection extends over the entire intra-hepatic portal system, and thence spreads to the lobules.

The appearance of the liver at this stage exactly resembles that described in Art. 480 as the condition of infiltration, and represented in

Fig. 180. The difference is merely that in the interlobular tissue and in the lobules we have accumulations not only of pigment or of leucocytes but also of formative cells and fibrous tissue varying in tint from grayish or reddish to yellow or greenish according to the amount of blood and of bile-pigment present. The yellow or greenish staining is most marked when the outflow of bile is hindered by the development of fibrous tissue and the retained bile stagnates and forms concretions in the ducts.

The lobules themselves may appear brownish-red, brown, yellow, or gray according as they contain more or less of blood or bile.

The enlargement of the liver by the growth of new fibrous tissue is sometimes so great that the weight rises to three or four kilogrammes (seven to nine pounds) or more. The condition might be aptly termed hyperplastic fibroid induration, but it is usually spoken of as '**hypertrophic cirrhosis.**' The surface of the liver is smooth, the tissue

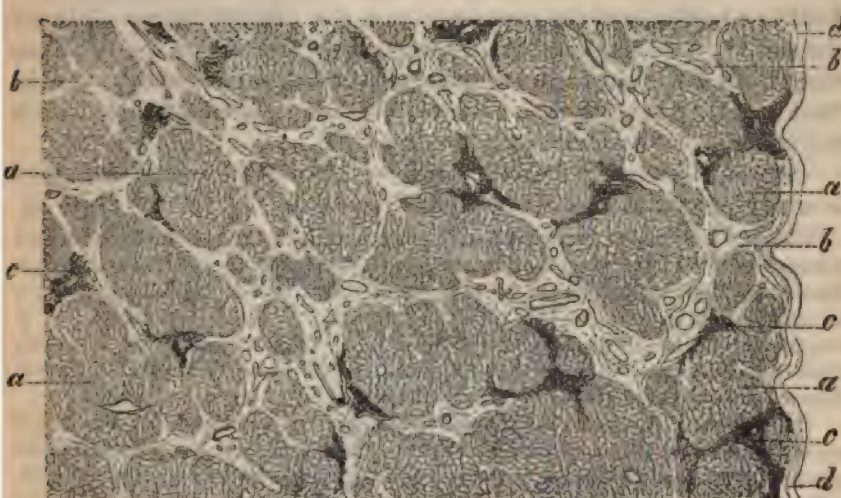


Fig. 192. Atrophic cirrhosis of the liver.

a, isolated patches of liver-tissue. *c*, cellular infiltration.
b, bands of vascular fibrous tissue. *d*, peritoneum.

dense and tough. When the lobules are invaded by the growth of fibrous tissue their outlines are indistinct or entirely lost.

The liver can of course become larger in this way only when the new fibrous tissue which is added more than counterbalances the liver-cells which are atrophied or destroyed. In many cases this is actually the case throughout, that is to say up to the death of the patient. But in other cases the progressive atrophy of the parenchyma is so great that the volume of the liver as a whole diminishes again.

When the fibrous overgrowth is at all extensive the diminution of volume is not so great as to reduce the size of the liver much below the

normal. This last is much more likely to happen when the change is from the beginning somewhat limited, affecting the interlobular tissue only, and not the whole of that.

In such a case the section of the liver shows at first nothing more than a number of bands or strands of fibrous tissue (Fig. 192 *b*) running through it; these are grayish-red or yellow or greenish, and enclose isolated patches of liver tissue that look yellow or gray or brownish as the case may be.

As the fibrous tissue shrinks and the liver-cells become atrophied, the liver at first more or less enlarged begins to contract. At the same time it becomes uneven and its surface is roughened, from the unequal shrinking of the fibrous bands (*b*) and of the remaining patches of liver-tissue. When these latter are small the section appears granular; when they are larger it is rather to be described as nodular or tuberculated or 'hobnailed.' When the fibrous overgrowth (and thus the contraction) is confined to a part only of the portal territory, the inequalities are of larger size and the liver may thus become lobulated. In extreme cases the volume of the shrunken organ is reduced by a half or two-thirds, and its form is at the same time gravely altered so that it becomes rolled up into a cylinder or flattened and tongue-shaped.

Interstitial hepatitis leading to contraction of the liver is described as **atrophic** or **Laennec's cirrhosis** (Fig. 191).

Chronic interstitial hepatitis has been much investigated during the last twenty or thirty years, and attempts have been made to distinguish various forms. SUKRE for example describes eight of these. Such classifications have no great scientific value, as the forms constantly pass one into another. It is enough to distinguish the hypertrophic conditions from the atrophic; and even then it must be borne in mind that these conditions merely represent different degrees or different stages of what is essentially one and the same process.

CHARCOT and GOMBAULT have contended that biliary hepatitis (Art. 498) always corresponds to the hypertrophic form; but this is incorrect, for inflammations starting from the bile-ducts do not always lead to hypertrophic induration (Art. 512), while the latter is often a result of inflammations starting from the portal vein or hepatic artery.

Jaundice, which may present or absent in cases of cirrhosis, does not by itself indicate either one form or the other; for both may in certain cases lead to retention of bile by obstruction of the smaller ducts.

References:—BRIGHT, *Medical Cases* London 1827, *Guy's Hosp. Rep.* 1836; BUDD, *Diseases of the liver* London 1857; FRERICHS, *Klinik d. Leberkrankheiten*, *Diseases of the liver* (New Syd. Soc. trans. by MURCHISON) London 1862; E. WAGNER, *Arch. d. Heilkunde* III.; LIEBERMEISTER, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten* Tübingen 1864; HABERSHON, *Guy's Hosp. Rep.* 1871; LAENNEC, *Traité de l'auscultation médiate* Paris 1826; CHARCOT, *Leçons sur les malad. du foie et des reins* Paris 1877; ZENKER, *Deutsch. Arch. f. klin. Med.* X.; CORNIL, *Arch. de physiol.* 1874; HAYEM, *ibid.* 1874; THIERFELDER, *Ziemssen's Cyclop.* IX., *Atlas d. path. Histologie*; JACCOUD, *Traité de path.* II.; BRIEGER, *Virch. Arch.* vol. [illegible]; [illegible], *Sammlung klin. Vorträge* no. 141; NICATI and RICHAUD, *Travaux du laboratoire de la rue des Fabres à Marseille* 1881; HAMILTON, *Journ. of anat. and physiol.* XIV.; CHARCOT and GOMBAULT, *Arch. de physiol.* 1876, *Leçons sur les*

maladies du foie, *Progrès médical* 1876, *Leçons sur diverses formes de sclérose hépatique* Paris 1879; SCHMIDT, *Zur path. Anat. d. Lebercirrhose* In. Diss. Bonn 1880; ACKERMANN, *Virch. Arch.* vol. 80; WYSS, *Virch. Arch.* vol. 85; HANOT, *Arch. générales de méd.* 1876; SURRE, *Etude sur diverses formes de sclérose hépatique* Paris 1879; POPOFF, *Virch. Arch.* vol. 81; POSNER, *ibid.* vol. 79; SIMONS, *Deutsch. Arch. f. klin. Med.* XXVII.; MANGELSDORF, *ibid.* XXXI.; BELOUSSOW, *Arch. f. exp. Path.* XIV.; LITTEN, *Charité-Annalen* V. (1878); FOÀ and SALVIOLI, *Arch. per le scienze med.* 1877; TEUFFEL, *Ueber hepatitis sequestrans* In. Diss. Tübingen 1878; CARL, *Ueber hepatitis sequestrans* In. Diss. Tübingen 1880; SABOURIN, *Revue de méd.* 1882 (finds that the intralobular veins are frequently occluded in cirrhosis); AUFRECHT, *Pathol. Mittheil.* II. (1883).

FOÀ, SALVIOLI, LITTEN, LEG, POPOFF, BELOUSSOW, and others have produced artificial hepatitis by ligature of the common bile-duct in dogs, rabbits, and guinea-pigs (Art. 513).

Syphilitic hepatitis.

498. **Acquired syphilis** may give rise to certain diffuse inflammatory changes in the liver, which from an anatomical point of view closely resemble the forms of cirrhosis we have just considered. The syphilitic nature of the lesions can therefore be determined only when other affections more characteristic of the disease are present.

But diffuse change of this kind is less common as a result of syphilis than are certain circumscribed and localized lesions, of which we seldom see anything but the terminal stages in the post-mortem room.

At various points, but chiefly in the neighborhood of the suspensory

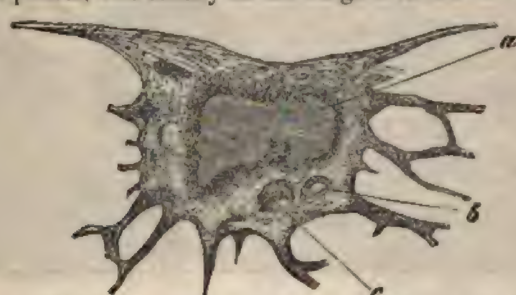


FIG. 193. GUMMA OF THE LIVER UNDERGOING CASEATION. (× 25.)

a, gumma enclosed in a capsule of scar-tissue.
b, artery with thickened wall. *c*, obliterated portal vein.

ligament, the surface of the liver is scarred and contracted or puckered, the peritoneal covering being thickened. If a section is made through one of these scars, we come upon a knot of dense fibrous tissue which sends radiating bands or branches into the surrounding liver-substance (Fig. 193).

The lobules included between these fibrous bands are brown and atrophied. As the centre of the node is approached the liver-tissue becomes less and less visible, being reduced to mere isolated patches and fragments (Fig. 194 *c*) and at length in the fibrous zone disappearing altogether. Sometimes this is all that is found, but in other cases the fibrous node

contains within it a caseous patch from the size of a pin's head to that of a cherry or larger. The patch if recent is surrounded by a gray semi-translucent areola of cellular tissue (Fig. 193). In the later stages it is directly enclosed by the fibrous zone, though isolated cellular foci may persist for a long time in the neighborhood of the node. Such a node is referred to as a gumma or gummatous node (Art. 130).

In rare cases two or more gummata are included in the same scar, and occasionally there is none at all. Similar gummata are met with also in the deeper parts of the liver; there may be as many as thirty or more of them. When the scars are numerous the liver becomes lobulated by their contraction.

As described in Art. 130 the centre of the node consists of homoge-

FIG. 194. SYPHILITIC SCAR AND GUMMA OF THE LIVER.

(*Hardened in alcohol, stained with alum-carmine, mounted in Canada balsam;* × 12.)

a, caseous centre.
b, zone of dense fibrous tissue.
c, fibrous tissue enclosing fragments of liver-tissue.
d. ramifying bands of fibrous tissue.
e, patch of semi-translucent cellular tissue.
f, cellular foci outside the fibrous zone.
g, normal liver-tissue.

neous denucleated necrotic tissue, or of granular detritus; the gray areola and the cellular foci are made up of granulomatous tissue. The materials in the centre are the remains of the liver-tissue infiltrated and destroyed in consequence of the syphilitic inflammation. The inflammatory process resulted primarily in the formation of a kind of granulation-tissue; but this was not completely transformed into new fibrous tissue, part of it becoming necrotic and ultimately caseous. The non-formative or rather destructive character of the syphilitic inflammation is due either

to some peculiar property of the syphilitic virus, or to the rapid occlusion of the smaller blood-vessels (portal and arterial) by specific endophlebitis and endarteritis.

500. **Congenital syphilis** also leads to hepatic disease. The affection takes the form either of cellular infiltration with more or less extensive fibroid induration, or of gummatous growths. These forms are met with not only in fœtuses and in infants who have died soon after birth, but also in young patients who in their infancy have not shown the signs of the disease.

When the cellular infiltration is slight the liver is not visibly altered, so far as can be made out by the naked eye. The microscope however readily proves the presence of extravasated leucocytes or granulation-cells. The interlobular tissue is usually the most affected, though infiltrated patches lying within the lobules are not uncommon. The leucocytes are often aggregated in greater numbers within the capillaries than outside them.

In marked contrast to this, the mildest variety of the affection, we occasionally meet with cases in which the whole liver is beset with new fibrous tissue, and thereby remarkably altered, enlarged, and indurated. The liver-substance is either uniformly pale or grayish-yellow, or of the color of flint (GUBLER) mottled with yellow, brown, and gray. The lobular structure is more or less indistinct, the cut surface having an even uniform structure.

The induration and enlargement are due to an abundant overgrowth of fibrous tissue, which extends with more or less uniformity not only along the portal sheaths but through the entire capillary network of the lobules.

The result is that the liver-cells, where they still survive, are for the most part shut off from their capillaries (Fig. 195) by a stratum of fibrous tissue either homogeneous and containing few cells or fibrillated and cellular. The liver-cells thus surrounded and enclosed are more or less atrophied and distorted; in some places they disappear altogether. At the same time the configuration of the capillary network is remarkably altered.

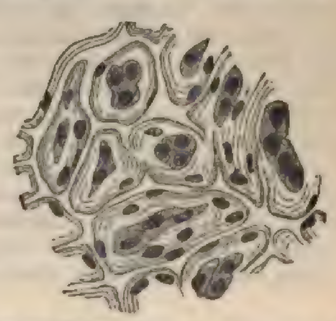


FIG. 195. DIFFUSE FIBROID INDURATION OF THE LIVER IN CONGENITAL SYPHILIS.

(From an injected preparation: × 150.)

The atrophied liver-cells are everywhere separated from the capillaries by a stratum of fibrous tissue.

This form of diffuse fibrous overgrowth leads to a hypertrophic cirrhosis of the liver in the manner already described; but certain other forms of induration occur in patients suffering from congenital syphilis which belong rather to the class of atrophic cirrhoses. There are also cases in which

the fibrous overgrowth is confined to the sheaths of the larger branches of the portal vein, and often reaches an extraordinary development. The fibrous tissue is sometimes highly cellular, sometimes not.

Gummatous hepatitis is another variety of syphilitic inflammation. It occurs in two forms, the miliary and the nodose.

Miliary gummata or syphilomata are simply small circumscribed foci of inflammatory infiltration, seated partly in the interlobular tissue, partly in the lobules. The affection is thus a special modification of the syphilitic hepatitis already described. The nodules are scattered through the entire liver, or confined to particular regions; in the latter case they are usually aggregated into groups and clusters. The single foci are punctiform, or it may be as large as a pin's head; when recent they are gray, but afterwards they turn yellowish-white or yellow. The intervening liver-tissue is either unaltered or affected with diffuse interstitial inflammation. Some of the liver-cells within the inflamed area are broken down or necrotic.

Nodose gummata are most frequently met with in patients who survive birth some months or years. When recent they form rounded or elongated and branched white patches with serrated or irregular margins. After a time the centre becomes caseous, and coarse cicatricial tissue forms about the periphery: as this contracts the surface of the liver is usually drawn in and puckered. The gummata of congenital syphilis are thus very similar to those of the acquired disease. When the liver is at all gravely affected by syphilitic hepatitis, inflammatory changes are induced in the capsule or serous covering (perihepatitis), which take the form either of simple exudations or of membranous adhesions to the surrounding parts.

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Tuberculosis of the liver.

501. **Tuberculosis** of the liver appears in two chief forms, namely as miliary tuberculosis and as tuberculous hepatitis.

The former is much more common than the latter, and is usually but a part of a general tuberculosis involving several organs or the entire body. The liver is beset with minute nodules, often so small as to be

scarcely perceptible, and gray, yellow, or bile-stained, as the case may be. The nodules lie either in the interlobular tissue or in the lobules or in both.

The nodules when recent consist of simple aggregations of small cells (Fig. 196 *b*); when more advanced they contain giant-cells; when 'mature' the central cells are denucleated and necrotic.

The most recent tubercles exactly resemble foci of simple inflammatory infiltration. The eruption of nodules is not infrequently accompanied by a diffuse and somewhat extensive cellular infiltration of the liver generally. Nodules of larger size are as a rule manifestly made up of smaller nodules.

As the tubercles become mature the infiltrated liver-tissue in which they are seated becomes necrosed and the cells are transformed into shapeless denucleated blocks. The bile-ducts sometimes perish in like manner. When they are surrounded or enclosed by tubercles the epithe-

FIG. 196. MILIARY TUBERCULOSIS OF THE LIVER.

(*Carmine staining:* × 150.)

a, mature tubercle. *b*, crude or recent tubercle.

lial cells, especially when they coalesce or fuse together, may simulate giant-cells. According to ARNOLD new bile-ducts may be formed in the midst of a tuberculous nodule, as in non-tuberculous interstitial hepatitis (Art. 497).

In the second form of tuberculosis, or chronic tuberculous hepatitis, there is not only an eruption of nodules but also a diffuse fibrous hyperplasia of the liver. Its tissue is traversed by more or less dense bands of fibrous tissue, containing small gray tubercles or larger yellow or bile-stained caseous patches. When these reach a considerable size they break down and cavities are formed, which enclose liquid or pulpy bile-stained

detritus. Cases occur in which the entire organ is honeycombed with innumerable cavities varying in size from that of a pea to that of a walnut; but such cases are rare. Large caseous nodes, resembling the solitary tubercles of the brain, are also rare.

References:—J. Arnold, *Virch. Arch.* vol. 80; Orth, *ibid.* vol. 60.

CHAPTER LXI.

TUMORS AND PARASITES OF THE LIVER.

Primary Tumors.

502. Both epithelial and connective-tissue tumors occur in the liver, but rarely as primary growths.

Of the epithelial tumors **adenoma** must first be considered, though it is a decidedly rare affection. It takes the form of multiple nodules, from the size of a millet-seed to that of a cherry, and grayish or yellowish or reddish on section. The smallest nodules are continuous with the surrounding liver-tissue, the larger ones are enclosed in a fibrous capsule and frequently undergo a process of internal softening.

When the adenomatous nodules are numerous the liver becomes greatly enlarged, and its surface is beset with rounded protuberances. Only one case is recorded (GREENFIELD) in which the tumor had given rise to metastatic growths.

The nodules consist of convoluted and anastomosing glandular tubes resembling the convoluted tubules of the kidney, and embedded in a framework of vascular fibrous tissue. According to RINDFLEISCH these tubes are developed from the cylindrical columns or trabeculæ of the liver-cells; the cells being supposed to multiply abnormally and to group themselves into tubular clusters. As the smaller nodules increase in size, fresh liver-cells are drawn into the growth, and the tubes already developed throw out fresh off-shots and branches.

References:—GRIESINGER, *Arch. d. Heilk.* v. (1864); RINDFLEISCH, *ibidem*; *Path. Histol.* vol. I.; GREENFIELD, *Trans. Path. Soc.* 1874; KELSCH and KIENER, *Arch. de physiol.* III. 1876 (with good figures); BIRCH-HIRSCHFELD, *Lehrb. d. path. Anat.* Leipzig 1877.

503. **Carcinoma** of the liver, as a primary growth, occurs in three chief forms.

In the first or nodose form, one or more nodes are formed, which may be seated in any part of the liver, but occur most commonly in the right lobe. The nodes are often of great size and cause the affected lobe to be much enlarged, the normal tissue being for the most part replaced by tumor-tissue. The nodes are usually globular and consist of soft or hard, white or slightly reddened tissue; the amount of cancer-juice which can be scraped from the cut surface varies much, and is sometimes very small indeed. At some points the tumor-tissue is sharply marked off from

the liver-tissue, the latter being manifestly compressed and distorted. At other points the tumor is continuous with the liver-tissue. The larger nodes are frequently softened or necrotic in the centre, or contain extravasated blood.

The second form has been well described as diffuse cancerous infiltration (or degeneration) of the liver. The organ is more or less enlarged, sometimes greatly enlarged, the serous capsule is thickened and tuberculated, much as in atrophic cirrhosis. On section also there is a resemblance to the cirrhotic liver, inasmuch as the whole organ is traversed and beset with anastomosing fibrous bands enclosing prominent islands of pale or reddish or bile-stained tissue. On examination these islands are seen to be carcinomatous in structure, and so the affection is distinguished from ordinary cirrhosis.

In the third form the cancerous growths are seated in the interlobular connective tissue. Wherever the portal vessels run they are seen to be

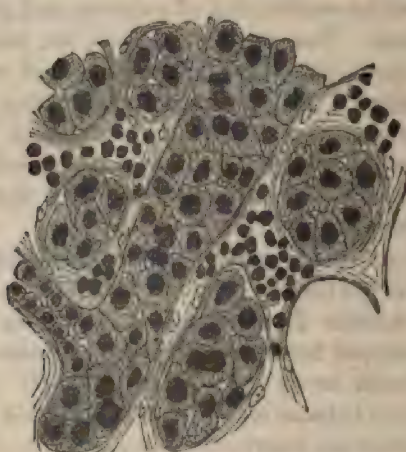


FIG. 197. CANCER OF THE BILE DUCTS.
(*Hæmatoxylin staining:* × 200.)
At the left side below a cancerous cell-nest is seen in communication with a bile-duct.

accompanied by white tumid nodules, in close mutual contact or actually coalescent, and varying in size with the size of the vessels. The smallest nodules are about the size of a millet-seed, the largest may be three to four centimetres across. The liver as a whole is of course greatly enlarged. The surface is smooth, as the nodules generally lie deep, only appearing (as white uneven protuberances) about the portal fissure.

None of the various forms of hepatic cancer show any marked peculiarity of structure (Fig. 197). The epithelial cells often form mere atypical clumps or nests; but cases occur in which they are arranged somewhat after the glandular type, the periphery of the nests being clothed with a layer of cylindrical cells. Sometimes too the alveoli of the fibrous stroma are simply lined with epithelial cells, without other

contents. So far as can be made out by examination of sections, it appears that the neoplastic epithelial growth may start either from the epithelium of the bile-ducts or from the liver-cells themselves. It is sometimes possible to make out an actual communication between the cell-nests and the unaltered bile-ducts (Fig. 197).

References:—PERLS, *Virch. Arch.* vol. 56; WEIGERT, *ibid.* vol. 67; SCHÜPPEL, *Arch. d. Heilk.* 1868, *Ziemssen's Cyclop.* IX.; NAUNYN, *Du Bois-Reymond's Arch.* 1866; WALDEYER, *Virch. Arch.* vol. 55; BIRCH-HIRSCHFELD, *Gerhardt's Handb. d. Kinderkr.* VIII.; WULFF, *Der prim. Leberkrebs* In. Diss. Tübingen 1876.

504. Primary connective-tissue growths are very rarely met with in the liver; but cavernous angioma or erectile tumor is not so uncommon.

Cavernous angiomata (Art. 150) form tumors as small as a millet-seed or as large as the fist, taking the place of a corresponding amount of liver-tissue. The liver is therefore not necessarily enlarged.

Angiomata lying close beneath the capsule appear as dark or livid spots; on section they are dark-red. In the larger tumors the cavernous

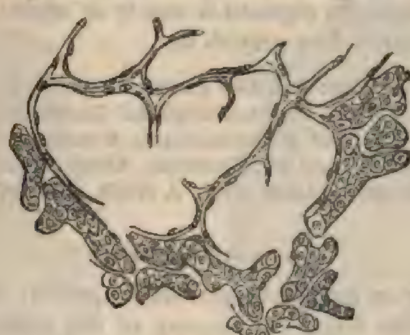


FIG. 198. SECTION FROM THE ADVANCING BORDER OF A VERY SMALL CAVERNOUS ANGIOMA OF THE LIVER. (× 150.)

or spongy texture is easily recognized, the pale fibrous septa contrasting with the blood contained in the meshes and cavities. The larger tumors again are bounded by a fibrous capsule, while the smaller are continuous with the liver-tissue.

As we have pointed out in Art. 150, the cavernous growth arises from a varicose dilatation of the capillaries of a lobule (Fig. 198), accompanied by the disappearance of the liver-cells. Proliferation of the intervascular connective tissue is a secondary phenomenon. The capsule of the larger tumors is formed essentially of the interlobular fibrous tissue surrounding the lobules. The intercavernous septa vary in thickness, but are usually thin and delicate.

Cavernous angioma is thus strictly speaking no true neoplasm; it is due primarily to a localized atrophy of the liver-cells. Accordingly we find it most frequently in the atrophied livers of aged patients. Not infrequently the tumors are multiple, the liver being beset with a multitude of cavernous patches of the most various sizes.

True connective-tissue tumors of the liver are as we have said very rare. Various forms have however been described, notably fibroma and sarcoma.

Some years ago the author met with a case in which the liver was beset, along the course of the sympathetic nerves, with a multitude of small firm **fibroneuromata**, from the size of a millet-seed to that of a bean. The patient in question had like fibroneuromata seated on all his nerves, except the olfactory and the optic.

Melanosarcoma (endothelioma melanodes, Art. 162) has also been observed. In a case recently examined the liver was greatly enlarged and thickly interspersed with grayish-brown and black growths of the most diverse forms and varying in size from that of a millet-seed to that of a walnut. To judge from the appearances presented by the smallest, the neoplastic growth started from the endothelium of the lobular capillaries, and gave rise to gradual atrophy of the liver-cells. The pigment lay chiefly within the tumor-cells, which were curiously irregular in shape. In some cases the pigment is scanty or absent in parts, and the tumor has there a whitish or grayish tint.

References:—On angioma: Art. 150; PAYNE, *Trans. Path. Soc.* 1869; STEFFEN, *Jahrb. d. Kinderheilk.* 1882. On lymphangioma: KLEBS, *Handb. d. path. Anat.* I. On primary sarcoma and melanosarcoma; ROKITANSKY, *Path. Anat.* III. FÖRSTER, *Illustr. med. Zeitung* III.; FRERICHS, *Klinik d. Leberkrankh.*, *Diseases of the liver* II. London 1862; BLOCK, *Arch. d. Heilk.* XVI. (1875).

Secondary tumors.

505. Secondary or metastatic growths, especially the cancerous, are very common in the liver. Carcinoma of the stomach, intestine, or pancreas is particularly apt to give rise to them, though they are not infrequent as a consequence of carcinoma of the œsophagus, uterus, or breast.

Cancerous metastases usually take the form of nodes, which vary much in number and sometimes pervade the entire liver. According to their stage of development they may be small, measuring only 11-20 mm., or so large as to measure 2–10 cm. in diameter.

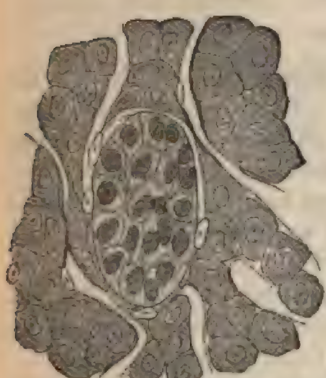
The smaller growths when they lie beneath the capsule appear as whitish patches, the larger project above the surface and are sometimes umbilicated. The overlying part of the capsule is usually congested and injected. When the nodes are both large and numerous the liver is enlarged, often enormously so, and its surface is uneven and tuberous. The nodes on the anterior edge can often be felt through the relaxed abdominal wall. On section the tumors appear white or yellowish-white with perhaps a tinge of red.

The centre of a large node is not uncommonly found to be opaque, fatty, and softened, so that scraping yields a pulpy mass rather than a juice. Caseous and hæmorrhagic patches are also met with.

The form of the primary carcinoma determines to a great extent the characters of the secondary growths. When the primary tumor (as in the stomach or intestine) is soft and medullary, the secondary tumors are also soft: they are hard and firm when the primary tumor (as in the pancreas or breast) is firm or scirrhous. Melanotic cancers give rise to brown or black metastases in the liver.

The surrounding liver-tissue is visibly compressed, and it may or may not be sharply marked off from the tumor-tissue. The smaller nodes are usually ill-defined, the larger ones are more distinctly circumscribed. But in this respect something depends on the structure of the tumor: the softer varieties are more apt to thrust back the surrounding tissue, the firmer usually infiltrate it.

The liver-tissue itself is brown, yellow, or yellowish-green, the last being a sign of retention or stagnation of bile. When the cancerous



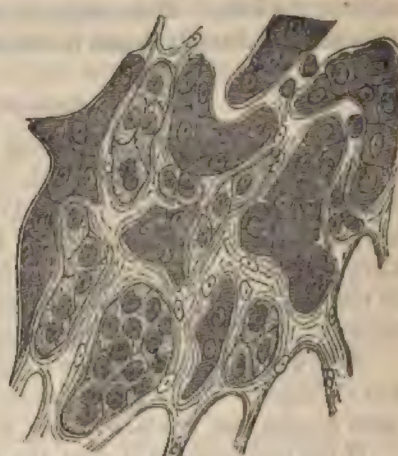


FIG. 199. CANCEROUS EMBOLUS IN A HEPATIC CAPILLARY.

(From a primary adenocarcinoma of the stomach: hæmatoxylin staining: × 300.)

FIG. 200. METASTATIC GROWTH OF CANCER IN A HEPATIC CAPILLARY.

(From a primary cancer of the pancreas: fibrous tissue is developing in the capillary; hæmatoxylin staining: × 250).

growths are numerous, the liver-tissue remains only in islands or narrow bands surrounded or encroached on by the advancing neoplastic tissue.

506. The **formation of** these **metastatic growths** is due to the invasion of the liver by germinal cancer-cells, which are brought to it by the blood-vessels, and (very rarely) by the lymphatics.

In by far the greater number of cases the germinal cells reach the liver by the portal vein. The places where the cells lodge and develop are in the smaller branches of the interlobular veins or in the capillaries of the lobules.

The first stage in the development that can be made out is the multiplication of the imported cells within the capillary where they have

lodged (Fig. 199). Then the capillary becomes distended by them, and the surrounding liver-tissue is compressed or thrust aside. As the nodule grows a new-formed fibrous stroma grows up among and between the cancer-cells, and separates them off into large and small clusters or nests, whose general grouping recalls the type of the mother-tumor. This fibrous stroma, which is vascular, is derived from the interlobular connective tissue of the liver. The liver-tissue either continues to be thrust aside, or is invaded, infiltrated, or permeated by the new growth.

The infiltration depends on the fact that fibrous tissue as well as cell-nests are developed within the capillaries (Fig. 200). The liver-cells surrounded and clasped by the new tissue presently become atrophied and disappear; before the last stage they often appear crammed with pigment granules.

Metastases derived from tumors not carcinomatous are rarely met with in the liver. Even sarcomatous nodules are not common, though they are occasionally found in children.

Animal parasites.

507. But few animal parasites take up their permanent abode in the human liver. The species which do so are—*Tænia echinococcus* (Arts. 245–248), *Distoma hepaticum* (Art. 237), *Distoma lanceolatum* (Art. 238), *Distoma hæmatobium* (Art. 239), *Pentastoma denticulatum* (Art. 225), and the *Psorospermia* (Art. 250). These have been fully described in the General Pathological Anatomy; here we propose merely to add something concerning the echinococcus or hydatid of the liver.

A **hydatid** has usually the form of a simple cyst, of the size of a walnut or larger. The wall is composed of an inner chitinous layer and an outer fibrous one, the latter being sometimes remarkably thickened.

If the echinococcus is alive the cyst contains a clear liquid, and the inner surface is covered with a whitish parenchymatous layer, on which are seated small white brood-capsules containing scolices (Art. 245).

Cases in which the mother-cyst is accompanied by internal or external daughter-cysts are less common.

By the time the liver comes to be examined the hydatid is usually dead, and the liquid wholly or partially absorbed. In this case the chitinous capsule is shrunken and folded, and contains a white cheesy, pulpy, or mortar-like and calcareous mass. In this the characteristic hooklets can often be discovered lying loosely. When the cysts reach a large size they may burst into the neighboring parts, for example, into the peritoneum or intestine, or externally; sometimes inflammation is set up around the cysts.

Echinococcus multilocularis, giving rise to what was formerly described as 'alveolar colloid' of the liver, is a peculiar variety described in Art. 247.

CHAPTER LXII.

THE GALL-BLADDER AND BILIARY DUCTS.

508. **Biliary concretions** and **gall-stones** are by far the commonest abnormalities in the contents of the gall-bladder and biliary ducts (hepatic, cystic, and common). They occur as a rule in elderly persons, more particularly in the gall-bladder. The concretions are friable granular yellow masses. The gall-stones or biliary calculi, which may be as small as a millet-seed or as large as a hen's egg, are rounded or ovoid, or angular and facetted. The latter is the case when several gall-stones have lain together in contact within the gall-bladder, the former when they have lain singly in the bladder or in one of the ducts.

The color, consistence, and density of the stones vary with their composition. As a rule they are somewhat soft, the surface pale grayish-white, yellowish, or brown deepening to black, and either smooth or rough as the case may be.

On section there is usually a dark-colored nucleus consisting of a combination of bile-pigment (bilirubin) and calcium-salts, surrounded by a lighter shell or crust containing crystalline plates of cholesterin radially disposed. The different species are distinguished according to the constituent which is most abundant.

(1) Stones consisting of **cholesterin.** These usually contain a pigmented nucleus, are single or multiple, grayish-white or yellowish-white in color, smooth or rough on the surface, slightly translucent, with sometimes a kind of pearly lustre. The fractured surface has a radiate crystalline appearance, and often shows traces of stratification. The stones are soft in texture. When stained with bile they are sometimes yellow or greenish or brown. When mixed with calcium-salts they are friable and chalky.

(2) Stones consisting of **cholesterin** and **pigment** are the commonest of all. According to the proportion of pigment they contain they are yellow, brown, black, or brownish-green. They are frequently present in enormous numbers and distend the bladder or ducts to a remarkable extent. They often contain a considerable amount of calcium carbonate and of magnesium-salts.

(3) Stones consisting of **bilirubin** and **calcium-salts,** or of biliverdin and calcium-salts, are rare and usually small.

(4) Stones consisting of **calcium carbonate** are very rare.

509. The exact way in which gall-stones are formed is not fully understood. In many cases foreign bodies are found within them, and we know that such bodies introduced into the biliary passages become crusted over. For example, a round-worm, which has crept into the common duct and there died, becomes covered with a coating of granular matters precipitated from the bile.

When the calcium-compounds and the cholesterin are dissolved out from a gall-stone, the insoluble residue is a nitrogenous body (HOPPE-SEYLER). It is probably derived from the remains of cast-off epithelium. No mucin can be detected, at least by chemical means.

Stagnation and decomposition of the bile seem to favor the formation of gall-stones. Certain conditions of the general nutrition are probably not without influence, seeing that the stones are much more common in patients of mature age than in younger patients.

Cholesterin is soluble in the sodium-compounds of the bile-acids, and thus a cholesterin-stone may be redissolved if the bile with which it comes in contact is not already saturated with cholesterin. The combinations of calcium-salts with the bile-pigments, on the other hand, are not soluble without actual decomposition (HOPPE-SEYLER).

510. The **effects** of the formation of **gall-stones** vary greatly in different cases. Often the wall of the gall-bladder is affected very slightly even when it contains a large number of stones.

Gall-stones give rise to very painful attacks (gall-stone or biliary **colic**) when they become impacted in the common or the cystic duct. Stones formed in the gall-bladder and in the ducts themselves are frequently discharged into the intestine through the common duct. But if one of these lodges or lingers in the duct, retention of the bile ensues; and this may give rise to dilatation of the ducts and to infiltration of the liver with bile. The liver-tissue may thereupon become degenerate or inflamed (Art. 512), while the parts around the impacted stone become also inflamed or even ulcerated. If the stone is near the mouth of the common duct the inflammation and ulceration may extend to the papilla at its mouth, and in this way set the stone free. Stones may escape from the gall-bladder into the intestine (duodenum or colon) directly : this of course can happen only when inflammatory adhesions have already been set up between the intestine and the gall-bladder. In unfavorable cases the stones break through into the peritoneal cavity or into the retroperitoneal tissue, or inflammation of the wall of the gall-bladder extends to the serous surface and peritonitis is induced.

When concretions form in the ducts within the liver, more or less intense inflammatory change is frequently set up around them. This change may be limited to an abundant cellular infiltration of the duct-wall and the adjoining tissue, which after a time leads to the formation of new fibrous tissue (Art. 496). Or when the retained bile becomes decomposed the inflammation often takes on a destructive character and

ends in an abscess; this again may break and lead to local or general peritonitis.

References :—BENEKE, *Deutsches Arch. f. klin. Med.* 1876; FIEDLER, *Jahresber. d. Gesell. f. Nat. und Heilk. zu Dresden* 1879; SCHÜPPEL, *Ziemssen's Cyclop.* IX., with full references; FRERICHS, *Leberkrankheiten, Diseases of the liver* II. London 1862; ROTH, *Correspondenzblatt f. Schweizer Aerzte* XI. (1881); PETERSSEN-BORSTEL, *Gallensteinbildung in ihrer Beziehung zu Krebs und Endarteritis chron.* In. Diss. Kiel 1883.

511. We said in the last Article that the bile-ducts sometimes become dilated behind an obstructing concretion. The seat and extent of the dilatation depend of course on the seat of obstruction. Closure of the common ducts leads to accumulation and stagnation of the bile in the gall-bladder as well as in the hepatic duct and its branches. Closure of one of these branches naturally affects the bile and the smaller ducts of the corresponding region and no other. A duct may be closed either by concretions forming within it, or by inflammatory growths or tumors in or near its wall. Parasites, such as the round-worm or the *Distoma*, sometimes creep into the ducts from the intestine, and occlude them.

The secretion which accumulates behind an obstruction is not always simply bile. When the cystic duct is occluded it is plain that no bile can collect in the gall-bladder. When therefore this becomes distended it is owing to the secretion of a mucous liquid from the mucus-glands in its lining membrane. This condition is described as **dropsy of the gall-bladder.** Something similar takes place in the ducts. When a portion of a duct containing mucus glands becomes abstricted, a mucous secretion may be poured out and distend it. **Cysts** of various sizes, and having smooth slimy walls, are thus formed within the liver. According to VON RECKLINGHAUSEN (*Virch. Arch.* vol. 84) this is the usual mode of origin of the small cysts which are found lying just beneath the serous membrane of the liver. In these cases there has at no time been any retention of bile; the *vasa aberrantia* of the biliary ducts (FERREIN) have simply become distended by the mucous secretion of their own glands. Some cysts of the liver are due to the distention of the lymphatics with accumulated lymph.

When no secretion is poured into a gall-bladder whose duct is obstructed, the normal contents sometimes become inspissated or even calcified. The bladder itself usually shrinks; while if inflammation is set up within it its walls may become notably thickened or in some parts ulcerated.

512. **Inflammation of the gall-bladder** (cholecystitis) and of the ducts has already been referred to in treating of interstitial hepatitis (Art. 498), and of the effects of biliary concretions. It is not an uncommon affection, and may be set up by the extension of an intestinal inflammation to the common duct and its branches, by stagnation or

decomposition of the bile, or by irritant matters brought to the mucous membrane by the blood.

Even the slighter forms may lead to obstruction of the ducts, retention of the bile, and **jaundice**; the obstruction being due to excessive mucous secretion or to swelling of the mucous membrane. In more intense or more chronic inflammations the exudation from the ducts and gall-bladder may be purulent. The connective tissues are thickly infiltrated; and not infrequently the capsule of Glisson round the hepatic duct, or the peritoneum round the gall-bladder, are likewise intensely inflamed. This last is especially the case when the primary inflammation is of a necrotic character accompanied by diphtheritic excoriation and ulceration. Within the liver purulent inflammations of this kind give rise to small abscesses containing liquid bile and biliary concretions. When such abscesses are formed in the gall-bladder or in the larger ducts outside the liver, or when they lie close beneath the capsule on its surface, they are very apt to cause peritonitis.

Chronic inflammation of the gall-bladder leads in general to thickening of its walls and to adhesions with the surrounding parts. The bladder frequently shrinks in consequence. The fibrous capsule around the ducts becomes in the like circumstances notably hyperplastic. Now and then the bladder and larger ducts appear beset with papillary outgrowths from the same cause.

When such an inflammationo f the ducts persists for a long time, or leads to persistent retention of the bile, the inflammatory changes extend to other parts of the liver. Brown or yellow granular biliary concretions appear in the interlobular tissue and within the lobules. The liver cells perish at various points; and inflammatory infiltrations appear within the lobules and terminate in abscess or in fibroid induration (Arts. 496–498).

Some authorities (SCHÜPPEL, TEUFFEL) have described the form of biliary hepatitis which terminates in abscess as *hepatitis sequestrans* (see Art. 498 for references).

Tumors of the gall-bladder and ducts are rare, **carcinoma** being the commonest form. As we have already pointed out (Art. 503) many cancers of the liver start in the smaller bile-ducts. Cancers of the gall-bladder begin as soft growths arising from the inner surface, which as they develop may extend to and invade the liver.

Destructive **adenoma** (adenocarcinoma) of the duodenum sometimes develops at or near the opening of the common duct, and may obstruct or altogether occlude the passage.

CHAPTER LXIII.

THE PANCREAS.

513. The **pancreas** is an acinous or tubulo-acinous gland, whose duct (canal of Wirsung) passes into the wall of the duodenum and there joins the common bile-duct, opening with it through a common orifice into the bowel. Only in rare cases has it a distinct orifice. The secretion of the pancreas, which is in effect an abdominal salivary gland, acts powerfully in promoting the digestion not only of starchy matters but also of albuminoids and of fat.

The morbid changes of the pancreas are seldom very marked; though it is liable to various affections both primary and secondary.

Of **anomalies** of development the presence of an accessory pancreas is the most noteworthy. This is a discoid structure, from the size of a lentil to that of a crown-piece, made up of glandular lobules, and seated on the wall of the upper part of the small intestine or of the stomach. It lies either close beneath the peritoneum, or more deeply embedded in the muscular or submucous layers. Its minute structure is exactly similar to that of the pancreas itself, and it communicates with the alimentary canal by a duct of its own.

The division of the pancreas into two equal or unequal lobes is much less common. The gland is entirely absent in various cases of imperfect development, where the whole body of the fœtus or the alimentary canal in particular is gravely malformed.

Hæmorrhage (pancreatic apoplexy) is not an infrequent occurrence in connection with the pancreas. When it occurs shortly before death the fibrous structures of the gland, and the neighboring parts, are found soaked with dark blood. More rarely a typical **hæmatoma** or blood-cyst is formed. When the hæmorrhage is less recent the infiltrated tissue has a brown or slaty tint.

These hæmorrhages are usually due to affections of the heart, lungs, or liver which give rise to engorgement of the abdominal veins. Cases however occur in which no such cause can be assigned, and in which we are constrained to assume that the cause is local; but it should be said that it is seldom possible to demonstrate this *post mortem.* Pancreatic hæmorrhage may prove fatal, probably from some depressant or other action upon the semilunar ganglia or solar plexus of sympathetic nerves.

Details of the morbid changes affecting the pancreas will be found in KLEBS's *Handb. d. path. Anat.* I., in FRIEDREICH'S Article in *Ziemssen's Cyclop.* VIII., and in ROBERTS'S Article in *Quain's Dict. of Med.* London 1882. KLEBS and FRIEDREICH give full references to the older and the more recent papers on the subject.

Pancreatic hæmorrhage is discussed by KLEBS (*op. cit.*), ZENKER (*Naturforscherversammlung in Breslau* 1874), CHALLAND and RUBONI (*Bull. de la soc. med. de la Suisse romande* 1877), PRINCE (*Boston med. and surg. Journ.* 1882), GUSSENBAUER (*Wiener med. Woch.* 13, 1883, *Medical Times* I. 1883). ZENKER describes three cases in which the hæmorrhage occurred in strong healthy men and speedily prove fatal.

514. **Atrophy** of the pancreas is met with in cases of general marasmus, and not infrequently in patients who have died of diabetes. The pressure of neighboring parts, and overgrowth of the interacinous connective and adipose tissue, may lead to atrophy of the gland-substance by compression. In simple atrophy the acini dwindle and in some places disappear entirely. The affected lobules may look quite normal in color, or they may be somewhat brown.

Fatty degeneration of the gland-cells is likewise met with, and is characterized by the yellowish-white tint it imparts to the parenchyma. It may begin as simple atrophy.

Lipomatosis or fatty infiltration of the gland as a whole is of a different nature. It is due to the transformation of the interacinous connective tissue into adipose tissue. It may be combined with a certain amount of glandular atrophy, so that in a sense the gland-cells may be said to be replaced by fat.

Amyloid degeneration of the vessels and connective tissue of the pancreas is not uncommon in association with amyloid disease in other organs. The gland-cells remain unaltered, or here and there undergo fatty degeneration.

Concretions are occasionally but not very often found in the pancreatic duct or its branches. They consist chiefly of calcium carbonate and phosphate. The smallest are as fine as grains of sand, the largest are about the size of a hazel-nut. They are usually round or ovoid, seldom angular or irregular in shape. The surface is sometimes smooth, sometimes uneven. Most of them are white or grayish-white, a few are distinctly gray or brown. They are commonly due to some interference with the free outflow of the secretion, and may occur in large numbers in the same patient. Inflammation is usually set up around them, and leads either to destruction of the gland-cells and induration of the connective tissue, or to suppuration and abscess.

When the pancreatic duct is occluded by concretions or inflammatory change or by a tumor, it becomes dilated behind the obstruction into a cylindrical, sacculate, or moniliform cyst or series of cysts: these have been described as **pancreatic ranulæ**, and sometimes reach a considerable size. The contents of the dilated duct are either pancreatic juice

with mucus, or pus, or a bloody liquid. In small cysts they now and then become inspissated and calcified. When indurative inflammation is set up around the cyst, the gland-cells often perish. Cystic dilatation of limited portions of the minor ducts is much less common: but it sometimes occurs at a number of points scattered through the gland.

On pancreatic concretions see VIRCHOW (*Verh. d. phys.-med. Gesell. zu Würzburg* II. 1852), FAUCONNEAU-DUFRÈSNE (*Traité de l'affection calculeuse du foie et du pancréas* Paris 1851), CURNOW (*Trans. Path. Soc.* 1873), JOHNSTON (*American Journ. of med. sciences* 1883, an admirably summary with full references).

On pancreatic cysts see ROKITANSKY (*Lehrb. d. path. Anat.* III. 1861), VIRCHOW (*loc. cit.*), VON RECKLINGHAUSEN (*Virch. Arch.* vol. 30), WYSS (*ibid.* vol. 36), KLEBS (*Handb. d. path. Anat.* I.), PEPPER (*Centralb. f. d. med. Wiss.* 1871), HJELT (*Schmidt's Jahrb.* 157, 1373).

515. **Inflammation** of the pancreas (pancreatitis) is on the whole a rare condition. Primary and secondary forms are distinguished according to their mode of origin. The former are the rarer and the cause of them often remains undiscovered: the latter are due to the extension of an existing inflammation in contiguous parts, or to a so-called metastasis from some remoter organ.

The slighest degree of inflammation is represented by the swelling of the pancreas occasionally met with in cases of infective disease, and notably in typhoid fever. It is due to an infiltration of the connective tissues with liquid and leucocytes, and in part to cloudy swelling of the gland-cells. When the affection is recent the gland is red and injected; in cases of some standing it is pale or even white.

In purulent or suppurative pancreatitis some portion, or the whole, of the interacinous (and often the peripancreatic) tissue is transformed into a dirty puriform mass. In later stages there are abscesses of various sizes. It is usually due to suppuration in some neighboring part, as in the lesser omental sac or in the common bile-duct: it is very rarely a primary affection.

Chronic indurative pancreatitis or **cirrhosis** is characterized by thickening and hardening of the connective tissue within the gland. The head of the pancreas is especially apt to be thus affected. When the gland-tissue is thereby destroyed and atrophied the organ as a whole becomes smaller. Indurative pancreatitis is most commonly secondary to inflammations of contiguous parts, such as the peritoneum, common bile-duct, or stomach (in gastric ulcer). In other cases the cause seems to be retention of the secretion or the presence of concretions in the duct. It is rare as a primary affection, though it is said to be sometimes a result of spirit-drinking (FRIEDREICH), and of syphilis congenital or acquired. In a few cases gummatous nodes have been observed.

Tuberculosis of the pancreas is very rare; though in cases of the general affection caseous nodules are occasionally met with in the gland. Tuberculosis of the lymphatic glands embraced or overlaid by the pancreas is less common.

Carcinoma is the chief of the primary tumors found in the pancreas. It usually gives rise to hard dense nodes seated in the head of the gland. Soft medullary and colloid cancers are rare, as are all forms affecting the middle part or the tail. Sometimes however a cancer starting in the head invades the whole gland, transforming it into a single tumor which may reach a great size. The cancerous infiltration may extend into the surrounding tissues, invading thus the common duct, duodenum, stomach, gall-bladder, spine, lymphatic glands, peritoneum, liver, etc. Numerous metastatic growths are frequently formed in the parts named. When the common bile-duct is attacked, retention of bile and jaundice may result; and the closure of the canal of Wirsung my lead to cystic dilatation of the secretory ducts in the tail of the gland. The adjacent veins, such as the vena cava, portal vein, and superior mesenteric vein, are sometimes encircled and gripped by the cancerous growth; the result is thrombosis or other serious disorder of the circulation.

Primary sarcoma of the pancreas is extremely rare.

Of secondary growths carcinoma is again the only form that needs to be mentioned. Cancer of the stomach and of the duodenum are those which most frequently induce the like in the pancreas. Metastases derived from cancer in more remote organs are much less common.

On pancreatitis see CRUVEILHIER (*Anatomie path.* part XV. vol. I.), KLOB (*Oesterr. Zeitschr. f. pract. Heilk.* VI. 1860), BIRCH-HIRSCHFELD (*Arch. d. Heilk.* 1875), NATHAN (*Medical Times* 2, 1870), CHIARI (*Wien. med. Woch.* 1876, 1880. *Med. Times* 1, 1880), FRAENKEL (*Zeitschr. f. klin. Med.*, 1882). CHIARI observed in several cases complete necrosis and separation of the pancreas. In one case the pancreas was entirely broken down, and escaping by a perforation into the intestine was passed *per anum*. This patient (who recovered) was suffering at the time from gall-stones, so it is possible that the suppurative inflammation of the pancreas was secondary to inflammation of the bile-duct.

On cancer of the pancreas see FRERICHS (*Klinik d. Leberkrankh. Diseases of the liver* I., London 1860), E. WAGNER (*Arch. d. Heilk.* 1861), LÜCKE and KLEBS (*Virch. Arch.* vol. 41), DAVIDSOHN (*Ueb. Krebs d. Bauchspeicheldrüse* In. Diss. Berlin 1872), STRÜMPELL (*Deutsch. Arch. f. klin. Med.* XXII.), MOORE (*St. Barth. Hosp. Rep.* 1881, 1882), LÖSCH (*St. Petersburg med. Woch.* 1883), WESENER (*Virch. Arch.* vol. 93), CHIARI (*Prag. med. Woch.* 1888, a case of secondary sarcoma).

SECTION IX.

THE URINARY ORGANS.

CHAPTER LXIV.

MALFORMATIONS OF THE URINARY ORGANS.

516. **The urinary organs** include the kidneys, the ureters, the bladder, and the urethra. The kidney is the secreting organ, by which water and a number of other substances are separated from the blood. The other organs named serve merely to convey the urinary secretion out of the body.

The development of the urinary organs is subject to certain abnormalities, but they are seldom such as to imperil life by preventing or seriously hindering the secretion and removal of the urine. The consequent malformations consist chiefly of deviations from the normal form, position, or number of particular parts: anomalies in the minute structure of the kidney are much more rare. Such anomalies, however, are of great importance, inasmuch as they may prove the starting-point for tumors of great size.

The post-embryonic disorders of the urinary apparatus affect either the kidney or some part of the urinary tract. Many of them continue to affect the part only in which they arise, while others extend by continuity to contiguous parts of the tract and in some cases ultimately affect the whole apparatus.

Most urinary disorders are hæmatogenous, *i. e.*, traceable to some disorder of the blood; and of all the urinary organs the kidney is most liable to be affected. Disease of the kidney or of the internal parts of the urinary channels is much less frequently the result of injurious agencies reaching them from the urethra. A third and not unimportant group of affections arise from the extension to the urinary organs of morbid processes affecting adjacent parts.

Development of the urinary organs. In man the urinary organs are derived from two distinct groups of structures which may be described respectively as embryonic and permanent (KÖLLIKER), or primary and secondary. The primary structures are the primordial kidneys or wolffian bodies, and the wolffian ducts.

The **wolffian duct** on each side arises from a columnar mass of cells (the intermediate cell-mass) lying between the lateral mass of the mesoblast and the anterior part of the protovertebral column. This mass presently becomes hollowed out into a duct opening posteriorly into that part (urogenital cloaca) of the

stalk of the allantois which lies within the body of the embryo, and which ultimately becomes the urinary bladder and the urachus.

The **wolffian body** arises independently of the wolffian duct from another part of the intermediate cell-mass. The mass breaks up into a number of transverse cords of cells appearing at first to be connected with the peritoneal epithelium. These cords speedily become excavated into cæcal tubules (wolffian tubes), which are more or less convoluted and ultimately open into the wolffian duct. The organ thus developed is not unlike the permanent kidney.

The secondary or **permanent kidney** and the ureter are later developments. The ureter arises as a dorsal diverticulum from the hind-end of the wolffian duct near its opening, the diverticulum growing forwards on the dorsal side of the wolffian body. The kidney is developed from the hindmost part of the intermediate cell-mass, the part namely that did not break up into wolffian tubes. The cells of the mass apply themselves to the growing ureter, and become excavated into tubules; collecting tubes spring simultaneously from the ureter, and becoming continuous with the former give rise to typical renal tubules. The ureter does not long remain attached to the wolffian duct, its opening being gradually carried back until it enters the cloaca independently. The renal tubules in the cell-mass become convoluted and round their cæcal ends appear small aggregations of cells, in which blood-vessels develop forming the vascular **glomeruli**. These glomeruli then push in or invaginate the renal tubules, and presently a series of spherical structures is produced, each consisting of a coil of convoluted blood-vessels almost entirely surrounded by a double envelope continuous with the wall of a renal tubule. The stalk or pedicle of the glomerulus passes out at the point where the original invagination took place, which is usually opposite to the starting-point of the tubule. This spherical structure so formed is the **malpighian body**, the spherical envelope being the **capsule** of Bowman. Meanwhile the tubules become elongated and convoluted, and are soon differentiated into the various segments recognized in the adult kidney.

In the human fœtus of eight weeks the kidney is already a lobulated organ with a number of completely-formed malpighian bodies. The papillæ (Art. 520) are apparent at the end of the third month, and some of the tubules have attained their permanent form by the fourth month. Glomeruli continue to be formed throughout the whole time of fœtal life and for some time after birth. The lobulated external form usually disappears during the first year of infancy.

The **bladder** is derived from the primitive urachus or stalk of the allantois, which arises in the first month from the hind-gut as a cæcal diverticulum lined with hypoblast. The urachus thus opens primarily into the terminal portion of the gut and afterwards becomes separable into two segments, the posterior forming the urogenital sinus or cloaca, the anterior being dilated into the bladder and receiving the ureters. In the second month the bladder appears as a spindle-shaped cavity communicating below with the anal portion of the gut and above through the still patent urachus with the umbilical cord. At a later stage the urachus contracts and ultimately closes into a solid cord—the median ligament of the bladder. The closure is not in all cases complete (LUSCHKA, *Virch. Arch.* vol. 23); even in adults it may persist as a fine tube communicating with the bladder and lined with epithelium.

References on the development of the urinary organs:—BALFOUR, *Comp. Embryology* II. ch. 23 London 1881 (with bibliography); KÖLLIKER, *Entwickelungsgeschichte* Leipzig 1879; FÜRBRINGER, *Morphol. Jahrbuch* IV. 1878; SEMPER, *Arbeiten a. d. zool. Inst.* II., III. Würzburg 1875–76; SPENGEL, *ibidem* III.; BRAUN, *ibidem* IV.; KUPFFER, *Arch. f. mikr. Anat.* I., II. (1865–66); KOWA-

LEWSKY, *Die Bildung d. Urogenitalanlage b. Hühnchenembryonen* Warsaw 1875; SEDGWICK, *Quart. J. Micro. Sci.* XXI. 1880–81; ALLEN THOMSON, *Quain's Anatomy* II. London 1882 (with full references).

517. Total **absence of the kidneys** occurs only in gravely malformed fœtuses, and is of course incompatible with independent life.

Absence of one kidney is rare in fœtuses otherwise well-developed. It does not interfere with growth and development, inasmuch as the other kidney becomes hypertrophied and assumes the whole work of excretion. The left kidney is more often wanting than the right. The corresponding suprarenal and ureter are usually absent, though in some instances rudiments of the lower extremity of the ureter have been found.

Congenital atrophy of one kidney is more common than entire absence. In well-marked cases the atrophied kidney appears as a thin plate of fibrous tissue 2–5 cm. in length and 1.5–3 cm. broad, with few or no traces of tubules or glomeruli, and supplied by renal vessels normal in position but abnormally small. Where the atrophy is less marked the remnants of renal tissue are more abundant.

The causes which determine the non-development of one of the kidneys are unknown. We can only say that for some reason the outgrowth from the primitive ureter out of which the kidney is fashioned has been hindered or altogether suppressed. Atrophy of the kidney must often originate in some similar condition of whose precise nature we are equally ignorant. In some cases however traces of inflammation, in the form of cellular infiltration and fibrous hyperplasia, are discoverable in the rudimentary organ. We are thus led to infer that intra-uterine inflammation of the kidney is possible and may lead to arrest of its development.

Among congenital **anomalies of form** the persistence of the fœtal lobulations is the most common. The boundaries of the renal segments are usually indicated by shallow furrows; it is very uncommon to find the furrows so deep that the segments are entirely separated into distinct *renculi*.

Cohesion of the two kidneys most frequently takes the form of the so-called '**horse-shoe kidney**,' in which the organs are found closer to each other than is normal and their lower ends are united by a band either of fibrous tissue or of ordinary renal tissue. Cohesion of the upper or middle parts is very much rarer. When the kidneys coalesce entirely into one there is usually very considerable misplacement of the organ. It is often seated just above the promontory of the sacrum in the form of a thick cake or disc, from the anterior aspect of which arises a single or double pelvis with from one to four short ureters. In a few cases the united kidneys have been found on one or other side of the spinal column.

The renal vessels of the united kidneys are always abnormal in their

origin, and are frequently multiple. Thus when the organ is just above the sacrum the arteries spring from the lower part of the aorta near its bifurcation, or from one of the common iliacs, while the veins enter the corresponding parts of the vena cava or iliac veins.

This abnormal cohesion and the malposition of the kidneys indicate that the primitive ureters or the corresponding cell-masses were checked in their growth forwards and came early into contact.

A normal or malformed single kidney, like the horse-shoe kidney, may be misplaced during development; this condition is referred to as **dystopia.** It occurs most frequently in the case of the left kidney, which approaches the middle line in the neighborhood of the sacrum. The renal vessels are abnormal in their origin and the ureter is shortened, but the corresponding suprarenal usually occupies its normal position in the abdomen.

The kidneys may in like manner be displaced after birth. The right is most often displaced: the cause is to be sought partly in some outward mechanical violence, partly in a loose or extensible condition of the peri-nephral structures, and especially of the peritoneum. The origin of the renal vessels in such cases is not necessarily abnormal, and the ureter is not abnormally short, though it may be twisted or otherwise disturbed. The kidney is moreover in general readily movable. When the mobility is due to the presence of a mesonephron, or peritoneal fold loosely attaching the kidney to the spine, the case is described as one of **floating kidney.** It is more common in women than in men, and on the right side than on the left. On congenital renal cysts and tumors see Arts. 551 and 556.

References:—RAYER, *Maladies d. reins* III. Paris 1839; HARE, *Med. Times and Gaz.* 1, 1858 and 1, 1860; ROLLET, *Die bewegliche Niere* Erlangen 1866; KLEBS, *Handb. d. path. Anat.* I. 1870; ROSENSTEIN, *Virch. Arch.* vol. 53; PERL, *ibid.* vol. 56 (with references); GRUBER, *ibid.* vols. 33, 68; BEUMER, *ibid.* vol. 72; SAWYER, *Floating kidney, Birmingham Med. Rev.* 1872; WÖLFLER, *Wien. med. Wochenschrift* 1876; Report, *Trans. Path. Soc.* XXVII. (1876); EBSTEIN, *Ziemssen's Cyclopædia.* XV. (1877); HERTZ, *Virch. Arch.* vol. 46; LANDAU, *Die Wanderniere d. Frauen* Berlin 1882, trans. by CHAMPNEYS (New Syd. Soc.) London 1884; NEWMAN, *Glasgow Med. Journal* August 1883 (with full bibliography); W. ROBERTS, *Urinary and renal diseases* London 1885.

518. **Malformations of the ureter** and pelvis of the kidney are met with both in normal and in malformed kidneys (Art. 517).

The commonest variety is the duplication on one or both sides of the pelvis and first part of the ureter. It is very rare for the pelvis to be further subdivided into a larger number of tube-like calices.

The duplication seldom extends throughout the whole length of the ureter so that the tubes open separately into the bladder. They usually run side by side, though cases are on record in which they appeared to cross each other.

Partial duplication of the ureter implies an early subdivision of the primitive diverticulum (Art. 516); complete duplication must be due to the simultaneous development of two diverticula from the wolffian duct.

Both normal and abnormal ureters may open in abnormal situations. In the male one ureter may open into the colliculus seminalis or into a seminal vesicle, in the female into the urethra, vagina, or uterus. A secondary coalescence of one ureter with the müllerian duct is sometimes observed.

In rare instances valvular folds of mucous membrane and twists or kinks in the tube may so obstruct the outflow of urine as to give rise to hydronephrosis (Art. 552).

Congenital atresia of a ureter or pelvis, or of a single calix, is rare.

References:—KLEBS, *loc. cit.*; HELLER, *Deut. Arch. f. klin. Med.* v.; WEIGERT, *Virch. Arch.* vol. 70; HOFFMANN, *Arch. d. Heilk.* XIII.; BOSTRÖM, *Beitr. z. path. Anat. d. Niere* Freiburg 1884.

519. Of the **malformations of the bladder** the most serious is extroversion (otherwise *fissura, ecstrophia,* or *inversio vesicæ*).

As was pointed out in Art. 9 this malformation is due to the imperfect closure of the abdominal walls and of the bladder: a defect remains above the symphysis through which the posterior wall of the bladder protrudes. The symphysis in many cases remains likewise unclosed, while the penis is rudimentary and the urethra opens on its upper surface (epispadias).

More rarely the bladder itself is closed and protrudes through the abdominal fissure or through the umbilicus (*ectopia vesicæ*). Sometimes the anterior wall is closed while the posterior remains open, a communication existing between the bladder and the pelvic cavity or the vagina.

Very frequently we find remains of the urachus in the round or median ligament of the bladder. They take the form of a narrow patent channel or of small detached cysts, which may be either closed or open toward the bladder. In the latter case they sometimes become distended with urine when the bladder is overfilled. If any impediment to the normal outflow of urine take place in infancy, the urachus may never close at all; and occasionally it has been known to serve as a means of emptying the bladder.

Division of the bladder into two separate or partly separate portions (*vesica bipartita* or *bilocularis*) is very rare: the two cavities may lie side by side or one above the other.

Congenital diverticula of the bladder are very rare.

Atresia of the vesical orifice of the urethra or of a ureter is also rare: in the former case, as we have said, the urachus remains patent.

Absence of the bladder unaccompanied by any other grave malformation is seldom observed; but it is more frequently found to be

abnormally small. When the bladder is absent the ureters open into the urethra.

Absence of the urethra occurs in both sexes: in females the bladder may open directly into the vagina.

Atresia of the urethra also occurs in both sexes, and is due either to defect of some part of the canal or to obliteration of its orifice.

The canal may be abnormally narrow either throughout or at some particular part (congenital stricture). The contraction is in some cases due to hypertrophy of the colliculus seminalis.

When the urethra opens on the upper aspect of the penis the condition is called **epispadias**, when it opens on the under aspect **hypospadias.** The latter is the more common: the orifice may be either in the penile portion, or in the anterior and even in the posterior attachment of the scrotum (*hypospadias perineoscrotalis*). The penis is usually small and stunted.

Occasionally we meet with cases in which the urethra has more than one external orifice: and in males the glans penis is sometimes pierced with what appears to be a second meatus, but is in reality a short passage ending cæcally.

CHAPTER LXV.

CLASSIFICATION OF RENAL DISORDERS.

520. **Structure of the kidney.** The kidney is a compound tubular gland by which water, certain salts, and nitrogenous waste-products are separated from the blood and excreted. Abnormal substances which have gained access to the blood are likewise in great measure removed from the body by this channel. The peculiar structure of the kidney corresponds with its function of separating these substances from the blood which circulates through it.

On section the kidney is seen to consist of two well-marked zones, the cortex without, the medulla within. The **cortex** forms a stratum from 8 to 10 mm. in thickness, enclosing the **medulla** which has the form of a number of rounded cones projecting inwardly, the free apices being known as **papillæ.**

These medullary cones or malpighian pyramids are made up chiefly of tubules and blood-vessels, whose general course is from the base to the apex. The number of tubules increases as we approach the base of a pyramid, partly because they subdivide, partly from the presence of tubules passing for a short distance into the pyramid from the cortex and then doubling back towards the cortex again. The latter tubules are slender and narrow, especially in the recurrent part; they are described as **Henle's loops**. The branching tubules are considerably wider and are known as the **collecting tubes.** The blood-vessels and the tubules are bound together by a small quantity of connective tissue containing lymphatic vessels.

The cortex is in the main made up of two distinct structural elements. The simpler structures are the so-called **medullary rays.** These are slightly conical portions passing up from the medulla and ceasing to be distinguishable only at the outer border of the cortex (Fig. 201 *B*): they are simply prolongations of the medullary substance and consist of like bundles of straight tubules (*k*). The vessels (*e*) of these rays are arranged in much the same manner as those of the medulla.

The tissue lying between the medullary rays is the true cortical substance or **labyrinth** (*A*), and consists essentially of a mass of tubules (*i*) of various sizes, together with blood-vessels whose peculiar course and configuration (*a b c d e f g h*) give the kidney its characteristic micro-

scopic appearance. The tubules and vessels are bound together by a scanty connective tissue.

The blood which reaches the kidney enters it by the branches of the renal artery at the boundary zone between the cortex and the medulla. The greater part of it passes thence through the interlobular arteries (*a*) which run in a zigzag course through the labyrinth towards the outer

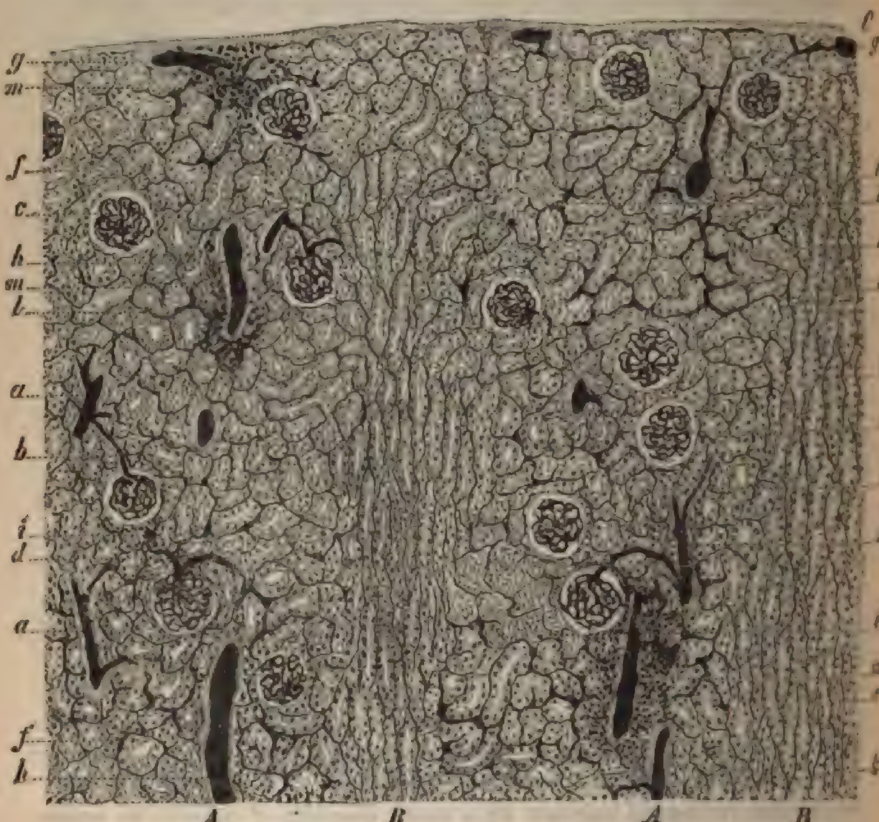


FIG. 291. SECTION THROUGH THE OUTER HALF OF THE CORTEX OF A KIDNEY AFFECTED BY RECENT INTERSTITIAL NEPHRITIS.

(*Arteries injected with gelatine and Prussian blue ; section stained with alum-carmine and mounted in Canada balsam ;* × 82)

A, labyrinth — *B*, medullary ray — *C*, capsule

a, interlobular artery
b, vas afferens
c, glomerulus
d, vas efferens
e, capillaries of the medullary ray
f, capillaries of the labyrinth
g, stellate veins
h, interlobular vein
i, convoluted tubules
k, straight tubules with Henle's loops and collecting tubes.
l, degenerated convoluted tubules
m, cellular infiltration round the interlobular veins

surface of the organ, and then by the vasa afferentia (*b*) to the glomeruli (*c*). Only a small part of the blood passes at once into the medullary

substance, and even this usually traverses a glomerulus. There are, however, certain very minute arterial twigs which pass directly into the medulla.

Within the **glomerulus** (*c*) the **vas afferens** breaks up into a multitude of anastomosing capillary loops, which presently reunite into a single vessel (*d*), the **vas efferens.** This leaves the glomerulus side by side with the afferent vessel, passes into the medullary ray, and there once more breaks up into a system of capillaries (*e*). This system (sometimes called the 'portal' system of the kidney) is continuous with the capillary system of the labyrinth (*f*), and this again delivers its blood into venules, which beginning beneath the capsule as **stellate veins** (*g*) pass through the labyrinth as **interlobular veins** (*h*) to the inner border of the cortex.

The course of a urinary tubule commences at the hollow sphere or **capsule** of Bowman which surrounds the glomerulus. At the pole opposite that through which the vessels enter, the cavity of the capsule opens by a somewhat narrow orifice into the lumen of the urinary tubule, which passes through the labyrinth as a comparatively wide **convoluted tubule** lined with a thick epithelial layer. The tubule then passes into the nearest medullary ray and descends with it in a straight course for a certain distance, then bending suddenly it turns back towards the cortex again. The descending limb of the **Henle's loop** thus formed is very slender and narrow, but the ascending limb widens out again, and at length enters a second wide convoluted tube (the **intercalary tube**) which lies in the cortical layer. The intercalary tube passes into a short and narrow **junctional tube,** and this uniting with others gives rise to the **collecting tubes.** These again unite together into the wider **excretory tubes,** which passing down through the medulla open at the papillæ into the **pelvis** or infundibulum of the kidney.

The glomeruli furnish chiefly the water of the urine. The convoluted tubules of the cortex secrete the solid constituents, namely the inorganic salts, urea, uric acid, hippuric acid, kreatinine, xanthine, sarkine, ammonia, coloring-matters, indican, oxalic acid, etc. Some of these substances (such as urea) are contained in the blood, others are elaborated in the kidney. It would appear that the epithelium of the tubules separates these substances from the blood and in an altered or unaltered form gives them up to the water flowing through the tubules from the glomeruli. A certain amount of osmotic diffusion also takes place between the secreted urine and the blood. Noxious substances in the blood, whether generated within the body or derived from without, are in great measure eliminated by the kidneys. In this way the kidneys act as purifying organs.

If a solution containing about 0.4 per cent of sodium sulphindigotate is injected into the external jugular vein of a dog, and the animal is killed a few minutes after, it is found that the coloring-matter is already in process of excre-

tion from the kidneys. According to HEIDENHAIN (*Pflüger's Arch.* vol. 9) and PAUTYNSKI (*Virch. Arch.* vol. 79) the excretion first begins in the convoluted tubules, the intercalary tubes, and the ascending limb of Henle's loops. The blue pigment appears in the form of granules in the striated epithelial cells, and stains both the free border and the nucleus. When excretion is in full activity small crystals appear in the cells. When the injection is made some time before death, and is followed by a second large injection of indigo-carmine, the vascular loops and epithelial cells of some of the glomeruli become stained. It thus appears that indigo-carmine may be excreted by the glomeruli.

When a solution of egg-albumen is injected (RUNEBERG, RIBBERT, and others), this substance is excreted by the glomeruli, and the same is true of hæmoglobin and sugar. These examples show that matters may pass into the urine both from the glomerular loops and from the intertubular capillaries, traversing in the process the epithelial lining of the glomeruli or of the urinary tubules (compare ADAMI, *Journ. of Physiol.* VI. 1885).

521. **Classification according to causation.** The morbid changes affecting the kidney may be appropriately grouped in five classes, according to their mode of origin.

First, we have those affections which are attributable simply to disturbances of the circulation.

Secondly, a group of changes produced by the deposit in the kidney of solid substances, brought to it as such by the blood or precipitated from their solutions.

A third group includes those degenerations and inflammations of the kidney which are due to impurities or disorders of the blood. As the kidney is one of the chief organs by which abnormal substances are eliminated from the blood, it is much exposed to disturbance of its own functions and even to lesions of its structure from this cause: and as a fact a very large number of renal disorders are thus produced.

A fourth group of disorders are traceable to injurious influences affecting the parenchyma of the kidney through the infundibulum. Thus mere obstruction of the outflow of the urine from the bladder may give rise to grave disorder of the kidney. The danger is of course greater when matters that are actively noxious reach the kidney by this route.

The fifth group comprises the tumors or new growths of the kidney.

COHNHEIM and ROY (*Virch. Arch.* vol. 92, *Proc. Camb. Phil. Soc.* IV. 1881) have investigated the mechanism of the renal circulation. They find that when a sensory or a splanchnic nerve is stimulated, in asphyxia, and in strychnine-poisoning, the volume of the kidney rapidly diminishes. When the renal artery on one side is tied, no effect is produced on the circulation of the other. When therefore in cases of loss of one kidney the other takes on the work of both, it is not due to a reflex action but to the effect produced on the circulation of the working kidney by the presence of urinary substances in the blood.

According to the experiments of RIBBERT (*Virch. Arch.* vol. 93) the quantity of urine excreted by a rabbit increases after the removal of the medullary cones. The view that water is re-absorbed from the urine as it passes through the medulla thus receives experimental corroboration.

CHAPTER LXVI.

DISORDERS OF THE RENAL CIRCULATION.

522. **Active hyperæmia** or congestion of the kidneys is due either to increased pressure within the aorta, or to dilatation of the renal arteries.

As the secretion of urine is in the main determined by the pressure and velocity of the blood flowing through the glomeruli, congestion of the kidneys is accompanied by an increase of secretion.

When one kidney is removed or rendered inactive by disease, the other carries on the urinary function unaided. This is of course possible only so long as its blood-supply is permanently increased. A kidney the demands on which are thus permanently increased presently becomes hypertrophied.

This **compensatory hypertrophy** is usually most extreme in cases where the other kidney has failed in early youth; in such cases the normal bulk may be increased as much as twofold. The increase is due chiefly to an increase in the length and calibre of the tubules and to enlargement of the glomeruli, in part also to a multiplication of both these elements. It is said however that multiplication is observed only in cases where one kidney has been lost before birth or in infancy.

Partial atrophy or destruction of a kidney may be followed by hyperæmia and consequent hypertrophy of the sound portion remaining.

The epithelial cells of the dilated and elongated tubules are larger and more numerous than is normal.

References on compensatory hypertrophy of the kidneys:—LEICHTENSTERN, *Berl. klin. Woch.* 24, 1881; GUDDEN, *Virch. Arch.* vol. 66; BEUMER, *ibid.* vol. 72; PERLS. *ibid.* vol. 56; RIBBERT, *ibid.* vol. 88; GRAWITZ and ISRAEL, *ibid.* vol. 77; EPPINGER, *Prag. med. Woch.* 36, 1879; BOSTRÖM, *Beiträge z. path. Anat. d. Niere* Freiburg 1884.

According to LEICHTENSTERN the diameter of a normal glomerulus measures 135-225 micromm., that of a convoluted tube 49-79 micromm., and that of a straight tubule 26-49 micromm. In hypertrophied kidneys the first measurement rises to 188-402, the second to 49-141, the third to 49-89 micromm.

The weight of the two kidneys (THOMA, *Untersuch. über die Bestandtheile des Körpers* Leipzig 1882) is in new-born infants about 23 grammes, at six months 44 gm., at twelve months 62 gm., at twenty years 285 gm., at twenty-five 304 gm. In the case of a healthy adult the two kidneys may differ in weight by as much as 30 to 40 gm.

523. **Passive hyperæmia** or engorgement of the kidney is usually the result of some general disturbance of the circulation; it is much less often due to local causes. Affections of the heart and lungs give rise to the former, compression and thrombosis of the vena cava or of the renal veins to the latter. Renal thrombosis most frequently occurs in infants of a few weeks old who die of general marasmus. Compression may be due to the gravid uterus or to an abdominal tumor.

If the outflow of blood from the kidneys is suddenly stopped, they become engorged and greatly swollen, assuming a dark brown or purple hue. Very soon hæmorrhages make their appearance, not only in the cortex and beneath the capsule but also in the medulla, Bowman's capsules and the urinary tubules becoming distended with blood.

If the obstruction of the renal veins is gradual, the blood in part finds its way into certain small vessels which pass from the kidney into the capsule and empty themselves into vessels communicating with the phrenic, lumbar, and suprarenal veins. In this way there may be little or no hæmorrhage within the kidney but only œdema, very few red blood-cells escaping from the vessels.

If however the obstruction is great and persistent the renal tissues become fatty and necrotic, and presently disintegrate entirely.

When the engorgement is less extreme, as in cases of uncompensated cardiac lesion, the swelling of the kidney is but slight, but its color becomes dark purple or cyanotic. If this condition persists for any length of time the kidney becomes remarkably dense and firm; at the same time the cortex becomes pale or grayish-red with darker streaks corresponding to the course of the veins. This change is referred to as **cyanotic induration.**

When the engorgement is still recent the vessels are uniformly distended with blood, the veins and capillaries being often greatly dilated. Within the capsule of many of the malpighian bodies and in the lumen of the urinary tubules appears a quantity of liquid, which on boiling yields a granular precipitate of albumen and often contains a few red blood-cells. In some of the tubes lie colorless transparent casts of the lumina, the so-called **hyaline tube-casts** or cylinders. These are simply masses of albumen which have escaped in liquid form with the watery transudation from the glomeruli, and have become solid within the tubules. Some of the epithelial cells, chiefly those of Henle's loops, contain brown and yellow and occasionally crystalline pigment-granules, derived from the coloring-matter of the blood-cells which have escaped into the tubules and there become dissolved. If the escape of red blood-cells from the glomerular vessels has been recent and unusually abundant the capsules of the malpighian bodies and the tubules connected with them may appear crammed with such pigmentary products of disintegration.

In cases of long-standing engorgement where the kidney is indurated,

the intertubular connective tissue is increased in amount, the blood-vessels are wide and flaccid, and the walls of the capillaries and the adventitia of the veins are thickened.

Many of the epithelial cells of the tubules are fatty and contain oil-globules of various sizes. The cells of the straight tubules of the medulla are especially liable to fatty change. The glomeruli appear for the most part unaltered; though here and there a malpighian body is seen whose contents have become homogeneous and shrunken, while the corresponding tubule is narrow, collapsed, or altogether atrophied (see Art. 525).

In engorgement of the kidney the urine is diminished in quantity. The albumen and red blood-cells it contains are derived, according to COHNHEIM and SENATOR, from the capillaries which surround the tubules, the exudation being simply the lymph of engorgement (Art. 24). At a later stage the glomeruli yield a similar albuminous exudation. COHNHEIM regards this as due in some measure to the altered relations of pressure, but in a greater degree to morbid changes in the excretory membrane, namely in the glomerular epithelium. RUNEBERG on the other hand refers the albuminuria of engorgement to a diminished difference of pressure between the contents of the glomerular vessels and those of the capsule of Bowman. This explanation is quite untenable in view of the experiments of BAMBERGER, NEWMAN and others.

References:—ROBINSON, *Med. chir. Trans.* XXV. (1843); JOHNSON, *Diseases of the kidney* London 1852; LITTEN and BUCHWALD, *Virch. Arch.* vol. 66; COHNHEIM, *Allg. Pathologie* II.; PERLS, *Arch. f. exp. Path.* VI.; HORTOLÈS, *Étude du processus histologique des néphrites* Paris 1881; LITTEN, *Untersuch. über d. hæmorrh. Infarct* Berlin 1877; TRAUBE, *Ges. Abhand.* I., II. (1871) and III. (1878); WEISSGERBER and PERLS, *Arch. f. exp. Path.* VI.; SENATOR, *Die Albuminurie* Berlin 1882, trans. by SMITH (New Syd. Soc.) London 1884; POSNER, *Virch. Arch.* vol. 79; HEIDENHAIN, *Hermann's Handb. d. Physiologie* V.; GERMONT, Thèse de Paris 1883; RUNEBERG, *Deutsch. Arch. f. klin. Med.* XXIII.; BAMBERGER, *Wien. med. Woch.* 1881; NEWMAN, *Journ. of Anat.* XII.; CORNIL and BRAULT, *Path. du rein* Paris 1884; ROBERTS, *Urinary and renal diseases* London 1885; VON NOORDEN, *D. Arch. f. klin. Med.* XXXVIII. (1886).

524. In general **anæmia**, and in contraction of the renal arteries by thickening or spasm of their walls, the blood-supply of the kidney is diminished, and it becomes anæmic. When the anæmia is considerable the organ becomes pale or grayish, and to some extent translucent. When the blood which reaches it is for any reason irregularly distributed the pale tint may appear mottled with redder patches.

The first result of renal anæmia is diminution of the urine; when the supply of arterial blood becomes very greatly diminished albuminuria appears. This occurs whether the anæmia be due to general causes (as in cholera), or to local arterial spasm (as in epilepsy, tetanus, asphyxia, pyrexia, or lead-poisoning). COHNHEIM regards it as due to ischæmic degeneration of the glomerular epithelium.

Transient anæmia gives rise to no demonstrable change in the renal structures, but in more chronic conditions degeneration and atrophy of

the tubules and glomeruli make their appearance. The deficient supply of blood and consequently of oxygen also leads to fatty change in the renal epithelium, which if it is at all extensive gives the section of the kidney a spotty or mottled appearance. If the blood-supply is entirely cut off general necrosis of the tissues ensues (Art. 527).

Slight but long-enduring interference with the blood-supply causes the essential elements of the kidney to dwindle and shrink, so that the bulk of the organ as a whole is gradually diminished.

525. Renal anæmia, in addition to the epithelial changes it induces, is very often accompanied by **atrophy** and **obliteration** of certain parts of the vascular system of the organ. These are most marked when they affect the glomerular capillaries.

A normal glomerulus (Fig. 202 *b*) appears as a tuft of capillary ves-

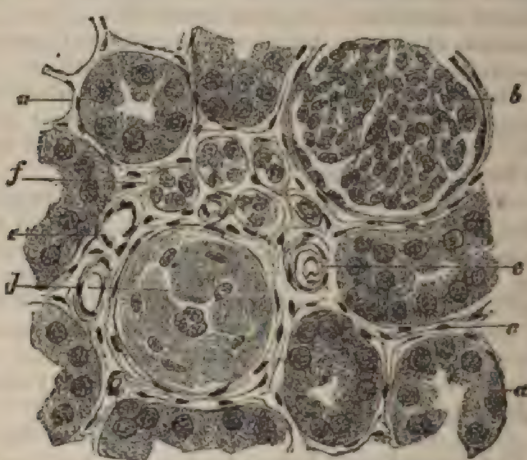


FIG. 202. SENILE ATROPHY OF THE KIDNEY.

(*Section hardened in alcohol, stained with alum-carmine, and mounted in Canada balsam:* × 100.)

a, normal tubule
b, normal glomerulus
c, vascular stroma
d, atrophied and functionless glomerulus
e, arteriole with somewhat thickened intima
f, atrophied and collapsed tubules

sels each covered with an investment of nucleated cells; those of an atrophied or functionless glomerulus on the other hand form a compact more or less homogeneous spherule with few nuclei or none (Fig. 202 *d*, Fig. 203 *b*). This spherule may show traces of lobulation, but the several capillary loops are no longer distinguishable. So far as we know, the steps of the change are collapse, thrombosis, and hyaline thickening of the capillary-walls; these latter then become fused into a homogeneous mass, the glomerular epithelium meanwhile disappearing. The capsular epithelium persists somewhat longer, but ultimately perishes in like manner, and the collapsed or shrunken capsule comes thus to

surround directly the altered glomerulus, without any intervening layer of epithelium (Fig. 203 *b*). The capsule itself is not usually altered: sometimes however a slight thickening takes place, and the wall then looks homogeneous or occasionally fibrillar in structure.

A glomerulus thus reduced to a homogeneous spherule is of course no longer permeable, and the vas afferens is either obliterated or delivers its blood directly to the vas efferens. The corresponding urinary tubule is also rendered functionless, and quickly becomes atrophied. The epithelial cells dwindle, lose their characteristic shape and striation, and are transformed into small cubical cells. They may remain as a regular lining or lie without order in the collapsed lumen of the tubule (Fig. 202 *f*, Fig. 203 *d*).

In some of the tubules the cells become entirely disintegrated (Fig. 203 *e*), or while diminished in size they become fatty, and sprinkled with oil-globules.

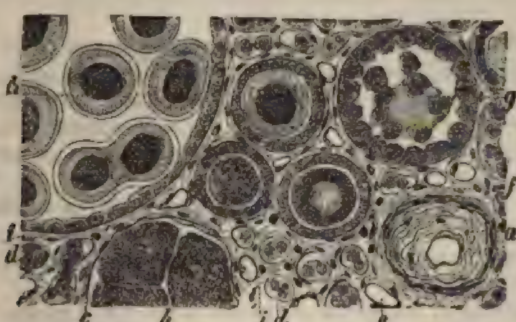


FIG. 203. CONTRACTED KIDNEY WITH ARTERIAL SCLEROSIS.
(Stained with alum-carmine, mounted in Canada balsam: × 150.)

a, artery with thickened and fibrous intima
b, obliterated glomerulus denuded of epithelium
c, capsule collapsed but not thickened
d, tubule collapsed and filled with small cells
e, tubule empty and collapsed
f, tubules with stratified and unstratified colloid casts and spherules
g, dilated tubule containing a homogeneous mass beset with shed epithelium
h, cyst containing stratified colloid spherules
i, stroma of cells and delicate fibres

In atrophic conditions the altered epithelial cells usually stain very deeply with the ordinary nucleus-staining reagents.

In the lumina of the functionless tubules, straight and convoluted, we frequently find homogeneous **colloid cylinders** and spherules (Fig. 203 *f h*). Some of these are stratified, others unstratified, and they may be so numerous as to distend the tubule into a small cyst (*h*). So far as can be made out with the microscope these homogeneous masses are a colloid product of the renal epithelium, which is produced either in the form of droplets that afterwards unite, or by a transformation of the entire cell when loosened from its place and carried to another part of the tubule (*g*). The dissolved albumen which flows through the

tubule as the degeneration of the glomerulus sets in may have something to do with its formation. When the lumen of a tubule becomes distended with these colloid masses the epithelium becomes flattened and compressed.

Larger colloid masses or agglomerations are visible to the naked eye as translucent yellowish or brownish jelly-like granules, from the size of a pin's head to that of a pea. In rare cases like masses are formed within the Bowman's capsule of the malpighian bodies.

The fibrous tissue of the atrophied region is not increased, but not infrequently there appears to be an accumulation of lymphoid cells in its meshes. It is questionable whether this is an inflammatory process; the impression conveyed is rather that the spaces left free by the collapse of the secreting structures have been partially filled up by indifferent cells.

COHNHEIM and MENDELSON (*Amer. Journ. med. sciences* Oct. 1883) have shown that in pyrexia the kidney becomes markedly anæmic from contraction of the renal vessels.

OVERBECK (*Wiener Sitzungsber.* XLVII.) and HERMANN (*ibid.* XXXVI., XLV.) have demonstrated that albuminuria results either from a short interruption or a considerable diminution of the circulation through the kidney. The albuminuria persists for some time after the circulation again becomes normal, and COHNHEIM thence argues that the cause is to be sought for in an alteration of the glomerular epithelium.

The vascular loops of the glomeruli are covered with a continuous layer of epithelial cells, which must be regarded as glandular in character, and make the glomerulus in effect a secreting gland. The secretion remains normal only so long as these cells are intact.

The great majority of the nuclei seen in the section of a glomerulus belong to these epithelial cells. The actual capillary-walls are either devoid of nuclei or possess very few indeed.

526. The simple atrophy of the glomeruli and tubules described in the last Article is met with in an uncomplicated form as a senile phenomenon: it is seldom absent in the **kidney of old age.** When the atrophied portions lie near the surface of the kidney they appear as small scar-like depressions, the surrounding parts of the parenchyma being somewhat redder than usual.

Simple atrophy of the secreting structures is also extremely common as an accompaniment of the most various renal affections. It occurs for example in embolic occlusion of the renal arteries, in the various forms of nephritis, and in hydronephrosis. We see it however in its purest form and greatest extension in the affection which is best described by the term **arteriosclerotic atrophy.**

The renal arteries and their branches in aged persons are very frequently the seat of sclerotic change (Art. 297), which may simultaneously affect the arteries of other regions also, or be confined to those of the kidney. The intima of the vessels thus becomes notably thickened (Fig.

203 *a*, Fig. 204 *e f*) and the lumen narrowed or obliterated: the result is that a certain number of glomeruli become more or less functionless, the number depending on the size of the affected arterial stem. Obstruction of a vas afferens will affect only a single glomerulus; constriction of an interlobular artery may cause the atrophy of an entire series.

The morbid changes appear in patches scattered over the kidney according to the distribution of the affected arteries; but occasionally they are so extensive as to affect almost uniformly the whole of the cortical zone.

FIG. 204. CORTEX OF AN ARTERIOSCLEROTIC CONTRACTED KIDNEY.

(*Arteries and glomeruli injected with Prussian blue; the section stained with alum-carmine:* × 50.)

a, normal glomeruli
b c, partially and totally atrophied glomeruli without thickening of the capsule
d, atrophied glomerulus with thickened capsule
e, artery with greatly thickened intima
f, interlobular arteries much convoluted and running parallel to the surface of the kidney
g, dilated arteries passing down to the medullary zone
h h_1, interlobular and subcapsular veins
i, large venous trunk
k, atrophied parenchyma with a few shrunken tubules *l*
m, cystic dilatation of a tubule with hyaline contents
n, normal tubules
o, tubules in the medullary ray with hyaline casts
p, patent tubules in the medullary ray
q, cellular infiltration

In slight cases the section shows only a few scattered cicatricial contractions of various sizes, which are usually somewhat redder than the parts around; these latter are pale grayish-red or reddish-brown in tint.

The greater the number of atrophic patches the more numerous are these cicatricial contractions, so that at length the kidney looks granular and roughened on its surface while its bulk is notably diminished. The condition may then be aptly referred to as **arteriosclerotic contraction.**

This form of contraction sometimes reaches an extreme degree, the whole kidney being remarkably small and shrunken, and the cortex reduced to a thickness of one or two millimetres. In such cases the greater number of the glomeruli are atrophied (Fig. 204 *b c d*), and the corresponding tubules (*l*) are collapsed, shrunken, and empty or filled with atrophied epithelial cells. Some of the tubules usually contain hyaline colloid masses, especially in the loops of Henle (*o*), which are often entirely filled with them. The convoluted tubules of the cortex on the contrary seldom contain casts, though here and there they appear dilated into little cysts (*m*) filled with colloid substance. Cases also occur in which the entire parenchyma is beset with small cysts from the size of a millet-seed to that of a pea. The shrinking and warping of the cortex causes the interlobular arteries (*f*) to be distorted and twisted into irregular spirals, while here and there some of them are so displaced as to run nearly parallel to the surface. Most of them show a more or less marked thickening of the intima (*e f*).

When the vascular system of the cortex is thus damaged or obliterated by the obstruction of the glomerular and interlobular capillaries the vessels running towards the medullary zone (the arteriæ rectæ (*g*)) become widely dilated, and the greater part of the blood-stream passes directly through the medulla.

In the arteriosclerotic kidney there is little or no hyperplasia of the connective tissue, and the capsule of Bowman is seldom perceptibly thickened. Here and there however the connective tissue shows patches of cellular infiltration (*q*).

GULL and SUTTON (*Med. chir. Trans.* LV. 1872) were the first to call special attention to the arterial changes associated with contracted kidney; they described the condition as 'arterio-capillary fibrosis.' Their statements were however somewhat lacking in precision, and they did not sufficiently distinguish between primary arteriosclerosis and the secondary form associated with interstitial nephritis. Dr. GEORGE JOHNSON (*Lectures on Bright's disease* London 1873) drew attention to the hypertrophy of the muscular coats of the arterioles in certain chronic kidney diseases; he interpreted the vascular change as secondary. In Germany THOMA and EWALD (*Virch. Arch.* vol. 71) minutely investigated the vascular changes in contracted kidney, but they too failed to keep distinct the various forms of the affection. ZIEGLER (*Deutsch. Arch. f. klin. Med.* XXV.) first discussed in detail the great importance of primary changes in the vessels in determining the contraction of the kidney, and showed that primary sclerosis gives rise to a special form of contraction, for which he accordingly suggested the term arteriosclerotic atrophy. LEYDEN has recently (*Zeitschr. f. klin. Med.* II.) and ROSENSTEIN (*Trans. internat. med. Congress* II. London 1882) examined the subject very fully, and proposes to call the affection renal sclerosis. ZIEGLER ob-

jects to this term on the ground that sclerosis of an organ implies induration, and the absence of induration in the arteriosclerotic kidney is what essentially distinguishes it from the cirrhotic contracted kidney. See also HOLSTI (*D. Arch. f. klin. Med.* XXXVIII. 1885), and GULL (*Amer. Journ. med. sci.* 1886).

The vascular change as we have seen begins usually in the arterioles. There is however evidence that the glomeruli may be the seat of primary sclerosis, the capillaries becoming obstructed by a hyaline thickening of their walls. It is worthy of note that arteriosclerotic contraction is very common among workers in **lead**, especially in the young; the sclerotic change is most marked in the smallest vessels and in the glomeruli. It would thus appear that lead has a selective degenerative action on these parts of the vascular system. The affection is usually accompanied by symptoms of gout. See OLLIVIER (*Archives générales de méd.* 1863), DANJOY (*ibid.* 1864), TRAUBE (*Allg. med. Centralzeitung* 1861). DICKINSON (*Diseases of the kidney* II. London 1877), HOFFA (*Ueb. Nephritis saturnina* Freiburg 1883), CHARCOT and GOMBAULT (*Arch. de Physiologie* 1881), WAGNER (*Ziemssen's Handb. d. spec. Path.* 3d edition IX.), GARROD (*Gout and Rheumatic gout* 3d edition London 1876).

Arteriosclerotic contraction is very gradual in its progress. Albuminuria is slight or absent altogether. Cardiac hypertrophy may ensue as in other atrophic affections of the kidney. For cases see LEMCKE (*Deut. Arch. f. klin. Med.* XXXV. with references), SCHUCHARDT (*Berl. klin. Woch.* 41, 1882).

527. The renal vessels having no arterial anastomoses, when a renal arteriole is blocked by an embolus **embolic infarction** ensues. Immediately after the stoppage of the circulation through the region supplied by the embolised vessel there is no apparent change in the renal tissue. In a few hours however the starved tissue dies, and gradually assumes a turbid grayish or yellowish tint. Presently there is more or less extensive hyperæmia and hæmorrhage and the pallor of the dead tissue disappears at least in part. LITTEN'S investigations show that the hæmorrhage takes place chiefly from the capillaries, and is in fact an extravasation from engorgement (Art. 30). The blood in the capillaries of the embolised region being derived solely from the neighboring capillaries the pressure is insufficient to drive it through them into the larger veins; stasis ensues, and soon the capillaries and venules are distended with blood, which at length escapes into the surrounding tissue. The extravasation takes place mainly from the intertubular capillaries, but blood-cells and plasma may escape from the glomeruli likewise and accumulate within the capsules and tubules. COHNHEIM and GUILLEBEAU have sought to make out that a certain amount of reflux takes place from the veins of the embolised region.

The hæmorrhage may be slight and limited to the marginal zone of the region, or it may be great and extend over the whole of it. In the latter case the entire patch becomes uniformly dark-red or mottled with red and gray. Very soon however this appearance changes, the centre of the patch becoming rapidly pale again by the diffusion and absorption of the coloring-matter of the blood. The infarct then closely resembles a simply anæmic patch.

In a few days after the embolism the infarct appears as a more or less regularly-shaped wedge or cone of a dull yellowish or grayish tint, surrounded by a zone of hæmorrhagic infiltration. Sometimes a narrow white zone intervenes between the latter and the pale centre. This white zone contains vessels filled with plasma and a great multitude of white blood-cells. The base of the cone is always directed outwards, and its apex is rounded off.

The size of the infarct depends on the size of the obstructed artery. The smallest may be no larger than a millet-seed; more commonly they are larger, measuring from 4 to 10 mm. at the base, and extending to the middle of the cortex or even to the boundary zone; now and then they are so large as to include a third or more of the whole kidney.

The renal epithelium perishes some two hours after the circulation ceases (LITTEN); it becomes homogeneous, or turbid and granular, and ceases to take up staining-reagents. The nuclei become pale and indistinct, and ultimately dissolve or break up into fragments. At first the dead cells retain their normal place and arrangement, but presently some of them break away from their attachment to the membrana propria of the tubule and are transformed into structureless flakes and blocks, or they crumble into amorphous granules. Sometimes a part of the necrosed and detached epithelium becomes calcified. Meanwhile the intertubular connective tissue swells, being pervaded with liquid and blood-cells or granular detritus. The former are met with chiefly in the red marginal zone, the latter in the pale centre. The nuclei of the connective tissue are pale and some of them lose their outline, while the membrana propria of the tubules is more or less swollen up.

The glomeruli remain for a considerable time unaltered, but by and by they too lose their nuclei and are transformed into colorless spherules in which the constituent parts are no longer distinguishable. When blood has escaped from the glomerular capillaries into the capsule and its tubule, the blood-cells may disintegrate into granular masses which form brownish casts of the lumen. But these are never numerous, and are often absent.

528. The changes just described take place of course only in the region where the tissue perishes, that is to say in the central parts and in a portion of the marginal zone of the infarct. This region gradually becomes disintegrated and liquefied, its structural elements losing their distinctness more or less completely. Even the fibrous structures and the glomeruli may in extreme cases break down and ultimately dissolve like the rest.

Notwithstanding this a focus of true colliquative softening is seldom produced, inasmuch as the products of disintegration and liquefaction are absorbed as fast as they appear. The epithelial cells are the only elements which disappear entirely over any considerable area, the fibrous tissue and glomeruli in great part remain undissolved, though of course

they are greatly altered. In the smaller infarcts no part of the fibrous structure entirely disappears.

The necrosis and disintegration of part of the tissue is accompanied by degenerative changes, chiefly fatty, of other parts. They are later in appearing, and affect the elements which do not at once undergo necrosis. The renal epithelium, the glomeruli and their capsules, and the fibrous stroma appear beset with oil-globules, though the fatty change never becomes extensive or extreme. Fatty degeneration may affect those glomeruli whose vessels remain intact as well as those where obstruction or obliteration has taken place. Collapsed and functionless tubules occasionally become distended with oil-globules, which may also make their appearance in the lumen of tubules that remain healthy.

Some portions of the embolised region may promptly receive a supply of blood from the neighboring capillaries or from the vessels of the capsule which penetrate the tissue of the organ (LITTEN, PAUTYNSKI). In other parts the interrupted circulation may in a few days be partially restored by the opening up of collateral channels, or of the obstructed vessel itself through shrinking or absorption of the embolus. The restoration of the circulation can hardly ever (at least in the larger infarcts) be sufficient to repair fully the damage done to the renal tissue. Some of the tubules and glomeruli always perish outright, or become so atrophied that they no longer perform their functions.

Complete restoration of an embolised region is in fact possible only when the normal circulation is very speedily re-established. If a glomerulus be permanently obstructed its tubule can no longer be restored to its normal state. If the conditions are so favorable that its epithelium once partially degenerated is reproduced by multiplication of the remaining cells, the new elements remain small and functionless. The same is true of the epithelial elements which do not perish outright, if the circulation through the corresponding glomerulus is permanently interrupted.

The loss of tissue brought about by the embolism results in the formation of a contracted cicatrix, which looks gray or reddish according to the blood it contains, and in later stages may become slaty-gray or brown from pigmentation.

In large infarcts extending through the whole thickness of the cortex the centre of the cicatrix shows no trace of renal structure, but is occupied entirely by fibrous tissue partly representing the original stroma and partly of new formation. Whitish fibrous nodules with few nuclei represent the glomeruli, the capsule of Bowman being no longer recognizable. There are no tubules, the only trace of their existence being clefts or streaks devoid of epithelium scattered through the cicatrix. The larger arterioles are collapsed and impermeable, and ill-defined against the surrounding fibrous tissue.

Surrounding the obliterated region is an irregular zone within which

the fibrous stroma is increased, the glomeruli reduced to homogeneous denucleated impermeable spherules, and the tubules collapsed.

The altered glomeruli are enclosed in a capsule which is either normal or consists of thickened fibrous tissue disposed in concentric strata: in recent infarcts the glomeruli may show a few scattered oil-globules. The tubules are either empty or contain small epithelial cells, usually lying without regular order in the lumen. Here and there towards the margin of the infarct tubules containing fatty epithelium are seen.

The intertubular fibrous tissue is always increased; in parts it is dense and coarsely fibrous, in others soft and beset with numerous round-cells. The latter are more numerous as the cicatrix is recent or imperfectly developed. Pigment is seldom present, though occasionally it appears in the form of granules and crystals.

The boundary between the cicatrix and the healthy tissue is seldom sharply defined, but the transition from normal to atrophied tissue is sufficiently clear. The neighboring healthy tubules sometimes contain hyaline casts.

The cicatrix is due to the absorption of the dead and degenerate tissue, which is only to a very slight extent regenerated, and to hyperplasia of the fibrous structures.

The number and magnitude of the embolic cicatrices determine the degree of distortion which the kidney as a whole undergoes by their contraction. When they are numerous and large the bulk of the organ may be considerably diminished, and a form of contracted kidney which we may appropriately call the **embolic contracted kidney** is produced. It is always characterized by the irregularity of the contraction.

Emboli containing infective matters give rise to metastatic abscesses (Art. 543).

References:—Kirkes, *Med. chir. Trans.* xxv. (1842); Beckmann, *Virch. Arch.* vol. 20; Cornil and Ranvier, *Man. d'hist. path.* Paris 1878; Arcatinzki, *Beiträge z. norm. u. path. Anat. d. Niere* 1877; Utthoff, *Exp. Beiträge z. Nephritis* In. Diss. Berlin 1881; Litten, *Zeitschr. f. klin.* Med. i. (1879), *Unters. üb. d. hæm. Infarct* Berlin 1879; Cohnheim, *Allg. Path.* i. Berlin 1882; Weigert, *Virch. Arch.* vols. 72, 79; Guillebeau, *Ueber d. Hist. d. hæm. Infarcte* Berne 1880; Grawitz and Israel, *Virch. Arch.* vol. 77; Talma, *Zeitschr. f. klin. Med.* ii. (1880); Pautynski, *Virch. Arch.* vol. 79; Hamilton, *Liverpool Med. chir. Journ.* July 1883 (who questions the existence of a hæmorrhagic stage); Mögling, *Zur Entstehung d. hæmorrhagischen Infarcts* Jena 1884 (with an admirable summary of the literature).

Litten has shown experimentally that the renal epithelium dies if deprived of blood for two hours. If the deprivation is of shorter duration it becomes for a time incapable of performing its functions. When the anæmia is maintained for six to eight hours the connective-tissue elements likewise perish. In rabbits and dogs the epithelium when killed by temporary ligature of the renal artery is in part detached from the tubules and forms epithelial casts which ultimately become calcified.

The urine secreted by a kidney in this state of anæmic degeneration and

necrosis is found to contain albumen. LITTEN holds that the albumen is derived from the degenerate epithelium, inasmuch as the glomeruli are apparently unaltered. This theory cannot be confuted, but it does not seem necessary, seeing that the admitted degeneration of the glomerular epithelium suffices to explain the escape of albuminous liquid from the capillaries. See also VON WERRA, *Virch. Arch.* vol. 88.

CHAPTER LXVII.

RENAL DEPOSITS DERIVED FROM THE BLOOD.

529. Deposits in the renal tissue of **solid or corpuscular matters** coming from the blood are of three kinds.

In the first place they may consist of foreign substances circulating in the blood. Secondly, they may consist of constituents of the blood which have abnormally escaped from the blood-vessels, in consequence of morbid changes in the parenchyma of the kidney. Thirdly, substances normal or morbid, which in health remain dissolved, may under special conditions be precipitated in the solid form within the kidney. In many cases two or all three of these forms of deposits are met with simultaneously.

Substances abnormally escaping from the blood-vessels are deposited in the fibrous stroma or in the tubules, whence they may ultimately reach the collecting tubes and the pelvis of the kidney. From the pelvis they may be at once carried off to the bladder, or they may remain for a considerable time.

Many deposits give rise to an appreciable alteration of the renal structures. Others induce more or less extensive degenerations, or inflammations. In this respect the behavior of bacteria reaching the kidney from the blood is very various. Anthrax-bacilli may crowd the renal vessels without giving rise to degenerative or inflammatory change, while the micrococci of pyæmia at once set up intense inflammation and wide-spread necrosis (Art. 543).

According to LITTEN bacteria may so multiply and accumulate in the Bowman's capsules and in the tubules as to distend them and effectually block them up.

530. **Leukæmic infiltration** of the kidney is one of the results of of leukæmia (Art. 260); it is characterized by an accumulation of white blood-cells in the renal tissue. When the infiltration is well marked the kidney becomes pale-gray in color and is somewhat swollen; or grayish nodules appear scattered through it.

See VIRCHOW (*Gessammelte Abhandl.* Frankfort 1856), FRIEDREICH (*Arch. f. path. Anat.* XII.), BÖTTCHER (*ibid.* XIV.), RINDFLEISCH (*Path. Hist.* II. London 1873), GREENFIELD (*Trans. Path. Soc.* XXIX. 1878).

Hæmorrhagic infiltration is usually due to extravasation of blood

from the glomeruli, or more rarely from the intertubular capillaries. As the blood escapes from the capsule of the malpighian body into its tubule (Art. 544, Fig. 213) the infiltration takes the form of reddened streaks and specks of the size of a millet-seed. Such extravasations are due partly to disturbances of the circulation, partly to alterations or degenerations of the glomeruli; but large hæmorrhages from the glomeruli are seldom due to mere disturbances of the circulation, except in the case of embolism. Blood which has escaped from a glomerulus, especially if it is considerable in quantity, usually becomes disintegrated within the tubules, forming granular yellowish or brownish casts of their lumina. After a time yellow or brown pigment granules also appear. As these lie chiefly within the epithelial cells (Art. 544, Fig. 213) we must apparently assume that the pigment is formed in the cells from the diffused coloring-matter of the blood. It is however possible that the cells may take up pigment-granules lying free within the tubules. This secondary condition is referred to as **pigmentary infiltration.**

Blood-cells, whether entire or disintegrated, which reach the pelvis of the kidney through the collecting tubes are in general speedily removed with the urine. It is only when a large intra-renal hæmorrhage has taken place, or when the mucous membrane of the pelvis itself is the source of the bleeding, that fibrinous coagula are produced, and then they take the form of tough dirty-white, yellow, or brown clots.

If as described in Art. 262 a solution of hæmoglobin in the blood-plasma has taken place, the dissolved hæmoglobin and methæmoglobin are excreted through the kidney (hæmoglobinuria). At the same time we find in the tubules deposits of lustrous reddish-yellow or brownish globules of hæmoglobin, yellow and brown pigment-granules, and less frequently red blood-crystals. This form is also described as pigmentary infiltration, but more fitly perhaps as **hæmoglobin infarction.**

The pigment-granules are partly deposited as such from the blood, partly precipitated from the dissolved coloring-matter in the process of excretion. In the deeper parts of the kidney these products of disintegration of the blood become aggregated into brownish granular tube-casts: the globules of hæmoglobin form homogeneous pale-yellow casts.

A third form of pigmentary deposit, **biliary infiltration,** is due to the precipitation of yellow or brown amorphous granules and flakes of bile-pigment. It is a result of icteric contamination of the blood. These granules lie for the most part within the epithelial cells, especially those of the convoluted tubules. Sometimes crystals of bilirubin are formed; this is most frequently observed in cases of *icterus neonatorum.*

These coloring-matters may give the kidney a dark-brown (from methæmoglobin) or a yellow or brownish-yellow tint (from bile-pigment). Deposits of amorphous and crystalline pigment appear to the eye as small reddish-brown to black, yellow, yellowish-brown, or yellowish-red

spots and streaks. In adults these are most numerous about the cortex, in infants chiefly in the medulla about the neighborhood of the papillæ.

A peculiar form of pigmentation, known as **argyrosis** or silver-staining, is due to the deposit of silver-particles in cases where preparations of the metal have been medicinally administered. The particles lie chiefly in the medullary zone, and give it a dark-gray tint.

Small hæmorrhages and pigmentary deposits cause no perceptible injury to the renal tissue. Larger hæmorrhages and extensive deposits of methæmoglobin and pigment may give rise to obstruction of the tubules and degeneration of the epithelium.

References:—PONFICK, *Berl. klin. Woch.* 17, 1876 and 46, 1877. *Virch. Arch.* vols. 62, 88; LESSER, *ibid.* vol. 79; MARCHAND, *ibid.* vol. 77; NEISSER, *Zeitschr. f. klin. Med.* I.; ADAMS, *Hæmoglobinausscheidung in den Nieren* In. Diss. Berlin 1880; BOSTRÖM, *Ueb. d. Intoxication durch d. essbare Morchel* Leipzig 1882, *Deut. Arch. f. klin. Med.* XXXII.; LEBEDEFF, *Virch. Arch.* vol. 91; LUCHSINGER, *Pflüger's Arch.* vol. 11; BÖHM, *Arch. f. exp. Path.* VI.; MASIUS, In. Diss. Breslau 1882; LICHTHEIM, *Sammlung klin. Vorträge* 134; JACOBI, *New York Med. Rec.* 11, 1879; DRESCHFELD, *Trans. internat. med. congress* I. London 1881; AFANASSIEW, and BOAS, *Arch. f. klin. Med.* VI. 1883, *Virch. Arch.* vol. 98.

After transfusion of blood from another animal (PANUM, PONFICK), after severe burns (PONFICK, LESSER, LICHTHEIM), poisoning with the morel mushroom (BOSTRÖM, PONFICK), and subcutaneous injection of glycerine (LUCHSINGER) hæmoglobinuria has been observed; and after poisoning with potassium chlorate methæmoglobinuria (MARCHAND, LEBEDEFF, JACOBI, DRESCHFELD). According to the recent researches of PONFICK (*Congress f. innere Medicin* Wiesbaden 1883) hæmoglobin is excreted not only by the glomeruli but also by the renal epithelium; see also ADAMI (*Journ. of Physiol.* VI. 1885).

The obscure affection known as intermittent or **paroxysmal hæmoglobinuria** appears to be associated with no recognizable anatomical alteration of the kidney other than hæmorrhagic and pigmentary infiltration and congestive hyperæmia. See the references in Art. 262; also MURRI, *Della emoglobinuria da freddo* Bologna 1880; COHNHEIM, *Allg. Path.* II. Berlin 1882; S. MACKENZIE, *Lancet* 1. 1884; DICKINSON, *Renal and urinary affections* III. London 1885; ROBERTS, *Urinary and renal diseases* London 1885.

531. **Uric acid,** whether produced in normal or abnormal quantity (as in gout), may be deposited in the kidney in the solid form or as solid urates when the water excreted is incapable of holding it all in solution. This is especially apt to take place (according to VOIT and HOFFMANN) when the urine becomes acid by fermentation, and acid sodium phosphate being present decomposes the alkaline urates of the urine to form basic phosphate.

The deposit consists partly of uric acid, partly of urates and especially sodium urate: it takes the form of amorphous granular masses or of acicular crystals. These lie in the tubules, chiefly the collecting tubules, and partly in the connective tissue.

The smallest deposits are not visible to the unaided eye. More

abundant precipitation gives rise to the powdery or coarsely granular deposits known as gravel or to renal calculi.

Uratic deposits are most frequently met with in new-born infants, especially such as die two to fourteen days after birth. In the first two days of life and in infants who have not breathed they are rarely found. Apparently the rapid metabolic changes which take place after birth are accompanied by the production of so much uric acid that the urine is incapable of holding it all in solution. These deposits in infants are sometimes described as **uratic infiltration**. They consist of ammonium and sodium urates; they lie in the medullary zone, and appear as pale yellowish-red streaks.

In adults the uratic deposits usually take the form of sand or **gravel**, and lie both in the cortex and the medulla, as well as in the calices and pelvis of the kidney: they vary greatly in amount in different cases. In the calices and pelvis they often become aggregated into concretions from the size of a pea to that of a hazel-nut, and are then known as **renal calculi**. Occasionally these take the form of large branching casts of the infundibulum and its ramifications, and then look something like masses of coral.

Uratic calculi are hard, yellow brown or red in color, and are smooth or slightly nodular on the surface. Small calculi have a crystalline fracture, but the larger ones are amorphous and often wood-like in texture. These deposits whether in the substance of the kidney or in its pelvis may give rise to disorders of secretion or to inflammation (Art. 555).

References on uratic deposits:—GARROD, *On gout and rheumatic gout* London 1876; HELLER, *Die Harnconcretionen* Vienna 1860; NEUBAUER and VOGEL, *Analyse d. Harns* Wiesbaden 1881; SALKOWSKI and LEUBE. *Die Lehre vom Harn* Berlin 1882; CHARCOT, *Leçons sur les maladies due foie et des reins* Paris 1877; COHNHEIM, *Allg. Path.* II. Berlin 1882; SENATOR, *Ziemssen's Cyclop.* XVI.; EBSTEIN, *ibid.* XV., and *Die Natur u. d. Behandlung d. Gicht* Wiesbaden 1882, trans. by SCOTT, London 1885; VIRCHOW, *Berl. klin. Woch.* 1884; DICKINSON, *Renal and urinary diseases* III. London 1885; RALFE, *Diseases of the kidneys* London 1885.

On uratic infiltration in infants:—VIRCHOW, *Gesammelte Abhandlungen* Frankfort 1856; SCHLOSSBERGER, *Arch. f. physiolog. Heilk.* IX. (1850); B. SCHULTZE, *Deutsche Klinik* 1858; RAPHAEL, *Brit. Med. Journ.* 1, 1870; LIMAN, *Handb. d. gerichtl. Med.* II. (1882).

According to the researches of CARTER (*Urinary calculi* London 1873), ORD (*Influence of colloids* London 1879), EBSTEIN (*Congress f. innere Med.* Wiesbaden 1883) all uratic concretions contain a colloid or albuminoid matrix, in which the various salts are deposited and by which they are cemented together.

532. Concretions of calcium phosphate and carbonate deposited in the kidney constitute what is called **calcareous infiltration**. It occurs chiefly in aged persons, in whom resorption of the bony structures is active; but it may occur without such resorption. The deposits are in the form of white grains, spherules, and nodules, and lie for the most

part in the looped tubules of the medullary zone, though some may be observed in the cortical tubules in the fibrous stroma, and even in the glomeruli.

Calcium phosphate may form gravel and small calculi in the pelvis of the kidney; the calculi are smooth and facetted, and of various degrees of hardness.

Calculi of calcium carbonate are very rare; they are brown or yellow and hard. This salt however not infrequently forms a constituent of other kinds of calculi.

Oxalic acid, whether ingested with the food or formed from the decomposition of uric acid, may be deposited in the kidney or its pelvis as 'dumb-bells' or octahedral crystals of calcium oxalate. This occurs when the amount of acid sodium phosphate in the urine is insufficient to maintain in solution the quantum of oxalic acid present. Within the kidney the oxalate forms white deposits. In the pelvis it forms pale or dark brown warty or spiny calculi. Pure oxalate calculi are very rare. The salt more frequently occurs as a constituent of uratic calculi.

Triple-phosphate of ammonium and magnesium occurs as soft crumbly white concretions, seldom pure, but frequently forming a coating on uratic calculi. The deposit is produced chiefly in ammoniacal decomposition of the urine; ammonium carbonate is first formed, and this precipitates the earthy and ammonium phosphates. The crystals of the triple-phosphate have usually the so-called 'sarcophagus-form,' derived from a rectangular prism by cutting off the angles and edges.

In rare cases renal concretions and calculi are found which consist of **cystine**, an abnormal constituent of the urine containing sulphur and crystallizing in hexagonal plates. They have rounded corners, are soft and wax-colored, and show a radiate crystalline fracture.

Xanthine calculi are extremely rare: they are pale or dark brown, very hard, and not unlike uratic calculi.

In one case (ORD, *Trans. Path. Soc.* XXIX. 1878) a concretion consisting chiefly of **indigo** has been found in the kidney.

All the forms of renal concretion and calculus may give rise to inflammation, and occur on one side or on both. The condition of a kidney containing a calculus in its pelvis is frequently referred to as **nephrolithiasis** (Art. 553).

References:—BENEKE, *Die Oxalurie* Göttingen 1852; NEUBAUER and VOGEL, *loc. cit.*; SALKOWSKI and LEUBE, *loc. cit.*; A. FRÄNKEL, *Zeitschr. f. klin. Med.* II.; LITTEN, *Virch. Arch.* vol. 80; ROBERTS, *loc. cit.*; WAGSTAFFE, *Trans. Path. Soc.* XIX. (1868); BEALE, *Urinary deposits* (plates) London 1883; DICKINSON, *loc. cit.*; ROBERTS, *loc. cit.*

LITTEN asserts that masses of micrococci within the glomeruli and tubules may become calcified. The calcareous deposit in the glomeruli, tubules, and renal epithelium may be so excessive that the function of the kidney is gravely interfered with.

533. When the glomeruli and their epithelium are seriously injured, or the circulation through them greatly disturbed, certain components of the blood may escape from their vessels which normally are held back. In like manner substances may escape from the intertubular capillaries into the tubules. This is most notably the case with regard to the **serum-albumen** of the blood, which in morbid conditions passes in greater or less amount into the urine (**albuminuria**).

This albumen comes from the glomeruli in the soluble form; but within the tubules it may coagulate and thus give rise to granular or homogeneous casts, especially in the region of the loops of Henle, but often in other parts also. These casts are known as **hyaline casts** or cylinders, and there is no doubt that they may consist exclusively of transuded serum-albumen, though they are also formed in other ways.

In many affections of the kidney, especially those of an inflammatory kind, the renal epithelium degenerates or breaks down and desquamates. Moreover we know that from the glomeruli and tubules there escape not only serum-albumen but also white blood-cells. In many morbid affections therefore the tubules contain not only soluble albumen but also albumen derived directly from the protoplasm of cells, and this albumen like the other may take part in the formation of tube-casts. In the first place, the desquamated epithelial cells become agglutinated into casts of the tubules: these have received the name of **epithelial casts.** So also the granular albuminoid and fatty products of their disintegration may in like manner give rise to **fatty casts.** Again the epithelial cells and leucocytes or their albuminous detritus may become transformed and fused into compact hyaline masses, or homogeneous masses may escape from the bodies of the degenerating cells and coalesce into homogeneous cylinders. Finally, both epithelial cells and extravasated leucocytes dissolve in the albuminous urine flowing through the tubules, and in this form play their part in the production of casts. The **granular casts** derived from blood-disintegration have already been spoken of (Art. 530).

Tube-casts may in certain circumstances be washed out of the tubules, and so escape from the kidney. The greater number however remain *in situ*, and are either redissolved or become more firm and dense so as somewhat to resemble wax (**waxy casts**). These occasionally give the reaction of the amyloid substance.

In addition to these casts, formed at least in part from transuded albumen, we may have homogeneous cylinders which are purely epithelial in their origin. These have been described in Art. 525 (Fig. 203) as **colloid casts.**

References on the formation of tube-casts:—BAYER, *Arch. d. Heilk.* 1868; AXEL KEY, *Schmidt's Jahrb.* vol. 114 (1867); BURKHART, *Die Harncylinder* Berlin 1874; AXEL KEY and LANGHANS, *Virch. Arch.* vol. 76; BARTELS, *Ziemssen's Cycl.* XV.; WEISSGERBER and PERLS, *Arch. f. exp. Path.* VI.; FINLAYSON, *Brit. For. Med. Rev.*

Jan. 1876 (on tube-casts without albuminuria); ROVIDA, *Moleschott's Untersuch* XI.; HUPPERT, *Virch. Arch.* vol. 59; RIBBERT, *Cent. f. med. Wiss.* 1879, *Nephritis u. Albuminurie* Bonn 1881; THOMAS, *Gerhardt's Handb. d. Kinderkrankh.* IV.; WEIGERT, *Sammlung klin. Vorträge* 162, 163; POSNER, *Cent. f. med. Wiss.* 1879, *Virch. Arch.* vol. 79; CORNIL, *Journ. de l'anat.* 1879, *Practitioner* XXVIII. (1882); SAUNDBY, *Birmingham Med. Review* Sep. 1883 (with references); KNOLL, *Zeitschr. f. Heilk.* V.

The formation of casts from epithelial cells has been specially investigated by LANGHANS. He showed that the glomerular epithelium may furnish the material. The cells are shed into the lumen of the capsule, reach the tubule, and break up into granular masses: these presently become clear and swell up, and coalesce into homogeneous cylinders.

CHAPTER LXVIII.

RENAL DEGENERATION AND NECROSIS.

534. When poisonous or otherwise noxious matters are excreted by the glomerular and renal epithelium, or when the nutrition of the renal tissue is impaired in consequence of changes in the blood or in the circulation, degenerative changes make their appearance in the glomeruli and tubules, and these changes are generally demonstrable by careful microscopic examination. The most frequent changes are—cloudy swelling, necrosis, and fatty degeneration.

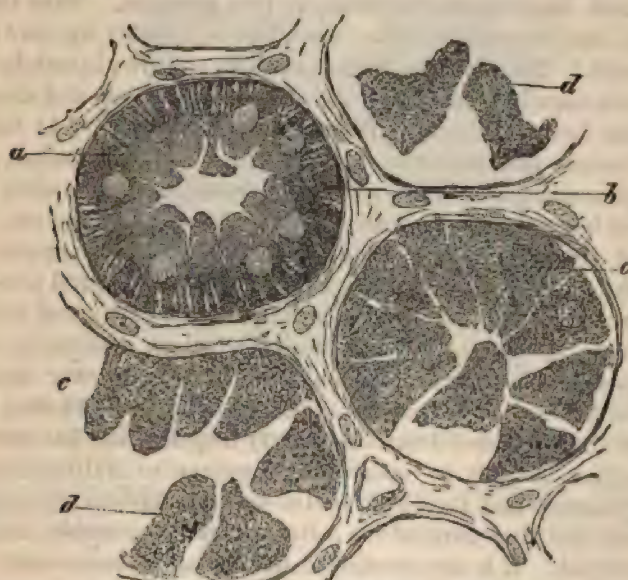


FIG. 205. CLOUDY SWELLING OF THE RENAL EPITHELIUM.
(*Preparation treated with chromic acid and ammonia:* × 800.)

a, normal epithelium — c, cells in extreme degeneration
b, cloudy swelling commencing — d, loose degenerate epithelium

Cloudy swelling. The epithelial cells (Fig. 205 *a*) of the convoluted tubules are usually wedge-shaped or conical; by broadening of the apex they may become more cylindrical, and by expansion of the base somewhat mushroom-shaped. The outer (parietal) half of each cell is striated with radial rod-shaped markings, due either to differentiation of

the cell-protoplasm into two substances of different refractive power, or to splitting and fibrillation. The inner (apical) half of the cell is homogeneous or finely granular, and in some cases terminates in a process (a), which ends in a free point or flattened plate, or joins with other projections, or simply lies over on the apex of the neighboring cell.

In the ascending limb of Henle's loops the cells are similar in form but somewhat shorter; in the descending limb the striated portion of the cell is contracted to a kind of basal plate. The epithelium of the intercalary tubules and collecting tubes is unstriated.

The condition known as cloudy swelling is accompanied by a slight enlargement of the kidney, the cortex assuming a turbid gray or grayish-red tint something like the tint of renal anæmia, but less translucent. If the interlobular veins contain blood the section appears streaked with red, while the medulla is generally livid.

When the affection first sets in the striated cells of the cortex become more markedly granular (*b*). The striations become less fine (NAUWERCK) and then appear to break up into granules. Then the apical part of the cell becomes granular, the whole cell swells up, and loses its normal shape. The processes become swollen, and are ultimately effaced. The nucleus soon becomes distended to a clear vesicle and disappears, and the cell looks uniformly turbid and granular (*c d*). At this stage the cells become loosened from each other, and somewhat raised up from their basal membrane. At length oil-globules may make their appearance in the body of the cell, which then breaks up and dissolves. In the convoluted tubules the first minute oil-globules usually appear at the bases of the cells; in the collecting tubes they appear round the nucleus (NAUWERCK). This series of changes is very frequently met with in infective fevers, such as typhus, small-pox, purulent meningitis, erysipelas, septicæmia, diphtheria, etc., and usually extends over the greater part of the cortex. If the change has not gone far the cells may recover; but where the associated dropsical or fatty degeneration has taken place the epithelium can only be replaced by regenerative multiplication.

The glomeruli and their epithelium usually show no visible change, though now and then some of the cells look swollen, turbid, and granular or powdered. It is also worthy of note that in some cases hemorrhage may occur from the glomeruli, distending their capsules and tubules with blood, and giving rise to red streaks and spots on the section of the cortex. These hemorrhages are due either to obstruction of the capillary circulation in the swollen parenchyma, or to degeneration of the glomeruli themselves. When the cloudy change has advanced to fatty degeneration in the tubular epithelium, that of the glomeruli and their capsules may also become fatty.

In the above account of the degenerative changes affecting the renal epithelium no reference has been made to the statements of other authors on the subject; the account rests solely on the observations made in ZIEGLER'S own labora-

tory in collaboration with NAUWERCK. In many memoirs on the subject no mention is made of the mode of preparation adopted, or hardening-fluids and reagents have been used which greatly alter the renal epithelium. Alcohol especially is entirely inadmissible in such investigations.

References:—KLEBS, *Hanb. d. path. Anat.*; RINDFLEISCH, *Path. Histology* II. (New Syd. Soc.) London 1873; PONFICK, *Berl. klin. Woch.* 1876–77, *Virch. Arch.* vol. 88; BOSTRÖM, *Ueber d. Intox. durch d. essbare Morchel* Leipzig 1882; BARTELS, *Ziemssen's Cyclop.* XV.; WAGNER, *ibid.* (3d German edition) IX.; BRAULT, *Journ. de l'anat.* XVI.; ECKSTEIN, *Deutsche med. Woch.* 1882; GAUCHER, *Lancet* 1, 1881; JACOBI, *Gerhardt's Handb. d. Kinderkrankh.* II.; THOMAS, *ibid.* IV.; WEIGERT, *Sammlung klin. Vorträge* 162, 163; MARCHAND, *Virch. Arch.* vol. 77; LEBEDEFF, *ibid.* vol. 91; P. FÜRBRINGER, *ibid.* vol. 91; LASSAR, *ibid.* vol. 77; NAUWERCK, *Beiträge z. Kenntniss d. Morbus Brightii* Jena 1884.

535. **Dropsical degeneration** of the renal tissue, and especially of the epithelium, plays a great part in the pathology of the kidney. The glomerular epithelium (Fig. 207) and that of the convoluted tubules

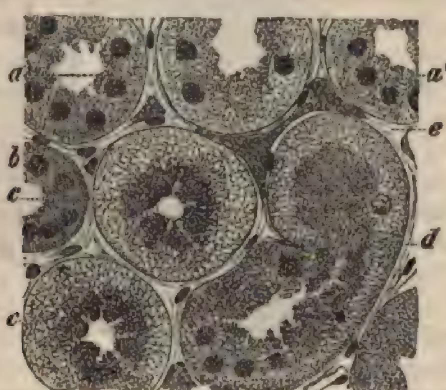


FIG. 206. NECROSIS OF THE TUBULAR EPITHELIUM IN *ICTERUS GRAVIS*.

(*Hardened in Müller's fluid, stained with gentian-violet, and mounted in Canada Balsam:* × 300.)

a, normal convoluted tubule
b, ascending limb of Henle's loop
c, convoluted tubules with necrosed epithelium
d, convoluted tubule with epithelium partly sound, and partly necrosed
e, unaltered stroma, with blood-vessels

(Fig. 206) is the most frequently affected, less frequently that of the straight tubules and collecting tubes. When the degeneration passes into **necrosis** the tubular epithelial cells become either turbid, or pale and homogeneous. The dropsical cells become greatly swollen, and clear spherules (so-called vacuoles) appear in their protoplasm: these are presently extruded or set free when the cell disintegrates.

Sometimes they coalesce to a frothy-looking mass. The nuclei of the cells sooner or later disappear (Fig. 206 *c d*), often before the form of the cells themselves is lost. This loss of the nucleus is due either to a process of swelling up and solution, or to disintegration into fragments. The

necrosed cells either break up *in situ*, or are first detached and then dissolve or disintegrate (Art. 533). Sometimes oil-globules may be seen in the necrosed epithelium.

When a portion of the tubular epithelium undergoes necrosis, similar changes are usually to be made out here and there in the glomerular epithelium also. Sometimes the changes are very marked. The cells swell up, are cast off (Fig. 207 e_1 e_2), lose their nuclei (e), and occasionally become vacuolated (e_3). Treatment of the sections with perosmic acid occasionally shows the necrosed epithelium to be studded with minute oil-globules. Ultimately the cells dissolve entirely, or with the exudation from the glomerular vessels form a granular coagulum (g). The denuded capillaries look pale and devoid of nuclei (d); they swell up and appear somewhat thickened. When the necrosis is total all the nuclei disappear.

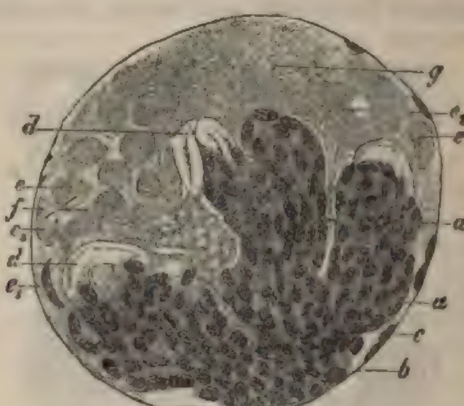


FIG. 207. NECROSIS OF GLOMERULAR EPITHELIUM AND EXUDATION INTO THE CAPSULE OF BOWMAN IN *ICTERUS GRAVIS.*

(*Hardened in Müller's fluid, stained with gentian-violet, and mounted in Canada Balsam.* × 300.)

a, normal capillary loop
b, capsule of Bowman
c, capsular epithelium
d, loop denuded of epithelium
e e_1 e_2 e_3, shed and degenerate glomerular epithelium
f, exudation between the epithelial cells
g, granular exudation and shed cells

The capsular epithelium undergoes necrosis much less frequently than that of the glomerulus, but cases occur in which it entirely perishes.

Necrosis of the renal epithelium appears as a primary affection chiefly in cases where the blood-supply of a region of the kidney is for a time interrupted, and when poisonous matters are excreted through it. Bile, cantharides, chromates, potassium chlorate, have this effect, which is also met with in various infective diseases, such as diphtheria, septicæmia, pyæmia, acute yellow atrophy of the liver, etc. It may be confined

to a few small parts, or be spread over a number of patches of considerable extent.

The cells of the vascular connective tissue are much less often affected by necrosis than the epithelial cells. NAUWERCK makes out that this happens most frequently in the case of the endothelium of the capillaries and venules, the cells of which are shed and transformed into pale homogeneous or finely granular masses, sometimes studded with minute spherules, and rounded, elongated, and sausage-like in shape. This change is not however confined to the kidney, but appears simultaneously in the vessels of other organs. Necrosis of the renal connective tissue is most common after long-persistent anæmia, in septic nephritis, and in cases of uratic deposit. The latter occurs in gout; indeed the formation of homogeneous necrotic patches beset with uratic crystals or granules has been held (EBSTEIN) to be the diagnostic mark of the **gouty kidney.**

Necrosis of the renal structures may also occur idiopathically, as it is called. If the loss of tissue be not great and confined to the epithelium, repair by regeneration is possible. Greater losses, or losses involving the connective tissue, result in permanent atrophy of the parts concerned (Arts. 527, 528). Calcareous salts are occasionally deposited in the necrotic patches, but this is rare.

The presence of necrotic tissue may induce inflammation in the contiguous tissue. In other and not infrequent cases the inflammation accompanies or even precedes the necrosis; the poison or other agent which causes necrosis in one part, acting as an irritant in another. This is exemplified in many bacterial affections of the kidney. Necrosis of the glomerular epithelium is always followed by transudation of albumen (Fig. 207 *g*), which coagulates when the section is treated with various reagents, and sometimes also during life (Art. 533).

According to FRERICHS diabetes is always associated with a "glycogenous degeneration" of the epithelium of Henle's loops, the cells swelling up and becoming hyaline. When treated with iodine brown-stained spherules and specks become visible in the protoplasm of the cells.

References:—WEIGERT, *Virch. Arch.* vol. 72; LASSAR, *ibid.* vol. 77; MARCHAND, *ibid.*; SCHACHOWA, *Untersuch. üb. d. Nieren* Berne 1876; CORNIL, *Gaz. méd. de Paris* 18, 1879 and *Journ. de l'anat.* 1879; FRÄNKEL, *Zeitschr. f. klin. Med.* II.; LITTEN, *ibid.* IV.; KOHN, *Berl. klin. Woch.* 1882; EBSTEIN, *Die Natur u. Behandlung d. Gicht* Wiesbaden 1882, *Deut. Arch. f. klin. Med.* XXVIII.; WINDLE, *Dublin Journ. med. sci.* 1883; FRERICHS, *Zeitschr. f. klin. Med.* VI. (1883), *Ueber den Diabetes* Berlin 1884; LEBEDEFF, *Virch. Arch.* vol. 91; ELIASCHOFF, *ibid.* vol. 94; AUFRECHT, *Pathol. Mittheil.* II. (1883); NAUWERCK, *Deutsche med. Woch.* 1884; Discussion, *Trans. Path. Soc.* XXXIV. 1883; INGLESSIS, *Le rein dans le diabète* Paris 1886.

536. **Fatty degeneration** of the kidney occurs under various conditions, and affects chiefly the epithelial structures.

In the first place, cloudy swelling (Art. 534) may issue in fatty change; or the latter may be associated with epithelial necrosis (Art. 535). Fatty change however is frequently met with as an independent affection, especially in chronic anæmia or engorgement, in many forms of poisoning (as with phosphorus or arsenic), and in infective diseases such as scarlatina, yellow fever, typhus, small-pox, etc. It may affect not only the tubular but also the glomerular and capsular epithelium, and is characterized by the formation within the cells of droplets of oil of various sizes (Art. 544, Fig. 213). When the degeneration is extreme the cells may become entirely disintegrated.

Slight fatty change is not perceptible to the unaided eye, especially when the vessels are full of blood, as in renal engorgement. Where the change is more marked the parenchyma assumes a grayish-white, white, or yellow tint.

In phosphorus-poisoning and in yellow fever the fatty degeneration may reach an extreme degree without other textural change. And in like manner we may have extreme fatty change uncomplicated with other conditions, the cause of which is as yet unrecognized. This is however rare, inasmuch as sooner or later inflammation is sure to be set up. A kidney which is uniformly of an opaque white through fatty transformation (**white or fatty kidney**) is always either inflamed or amyloid in some degree.

The inflammatory condition is in many cases secondary to the fatty change (as in anæmia, phosphorus poisoning, and yellow fever). In other cases it is antecedent or concomitant; so that the process is throughout inflammatory, and the fatty change is to be regarded as an accompaniment or result of the inflammation (Art. 544).

Fatty change may issue in complete recovery if the initiating cause be checked or removed, the lost epithelium being replaced by regenerative multiplication of the uninjured cells. This is especially true of non-inflammatory change, inflammatory conditions leading in general to destruction or atrophy of the tissues. It is of course immaterial whether the inflammation is primary or secondary.

Degeneration of the vascular connective tissue occurs to a serious extent only in cases where there is simultaneously a wide-spread degeneration of the epithelial structures; it is most marked in the inflammatory varieties. The capillaries are in general the most affected, their endothelium at times appearing crammed with oil-globules.

In the fibrous structures the connective-tissue cells are the parts which become fatty. The droplets of oil met with in the meshes of the tissue are for the most part derived by absorption from the affected tubules.

References:—Bartels, *loc. sit.*; Weigert, *loc. cit.*; Cornil and Brault, *Journ. de l'anat.*; XVIII. (1882), *Practitioner* XXXII. (1882); Charcot, *Leçons sur*

les maladies du foie et des reins Paris 1877; JOHNSON, *Med. chir. Trans.* XLII. (1853); WHIPHAM and others, *Trans. Path. Soc.* X., XIII., XIX.; RICKARDS, *Brit. Med. Journ.* 2, 1883.

537. **Amyloid degeneration** of the kidney often appears in what is known as the "**large white kidney**;" it may however in other cases present an appearance that has little in common with this form.

Slight degrees of the affection frequently give rise to no characteristic change. The cortex may be more or less red according to the quantity of blood it contains; but it is usually paler and softer than in health, and somewhat yellow. If the change is greater the cortex is generally pale and anæmic, with a grayish or yellowish tint, and more or less swollen. The color is also rather spotty, numerous small white opaque patches being sprinkled over a grayish-white translucent ground. The interlobular veins, if distended with blood, may cause the cortex to be streaked with red. The glomeruli are seen as pale or reddened nodules, occasionally somewhat translucent. The medullary zone is usually streaked with red, but it is not infrequently pale. The surface of the kidney is smooth, or here and there slightly granular and shrunken.

In a third variety, where the amyloid change has reached its highest intensity, the kidney is also pale and spotted with white or yellow, but its consistence is much denser and firmer than in the second variety. On section a number of semi-translucent patches and streaks appear, looking like bits of boiled bacon, and scattered through the medulla as well as the cortex. In extreme cases these may coalesce into continuous areas. Between the soft and the hard (or lardaceous) amyloid kidney there are of course many transitional forms.

The white patches are due to fatty degeneration, which always accompanies the amyloid change, but varies much in its extent.

Simple amyloid change gives the renal tissue the semi-translucent lardaceous aspect, which is well seen in the larger continuous patches. It affects first of all the glomerular capillaries, whose walls become thickened and homogeneous (Fig. 208 *b*). At first the altered patches are scattered irregularly, but soon they coalesce so that at length the entire glomerulus is transformed into an aggregation of homogeneous flakes or blocks. When the degeneration is complete the vessels become impermeable.

After the glomeruli the parts most affected are the walls of the vasa afferentia (*i*) and interlobular arteries, and those of the vessels of the medullary zone. Lastly the change may extend over the greater part of the venous and capillary system of the cortex, and even attack the membrana propria of the urinary tubules. These parts all become thickened, homogeneous, and translucent, and yield the familiar amyloid reactions.

The whole of the epithelial elements of the kidney—tubular, glomerular, and capsular—may simultaneously become more or less fatty

(*d e f*). The extension of the fatty change is not proportionate to that of the amyloid change: it may be extreme when the latter is slight, and inversely.

The convoluted tubules are frequently the most affected. Their epithelium is not only fatty, but loosened and disintegrated (*f*). When this change is marked, and some of the glomeruli become at the same time impermeable, small patches of the renal parenchyma may atrophy and disappear, and so give rise to contractions. If these lie near the surface they appear as small cicatricial depressions.

The loose epithelial cells naturally fall into the lumen of the tubules, and may there form cylindrical masses of fatty cells or fatty detritus. Others of the tubules contain hyaline cylinders, which are soft and

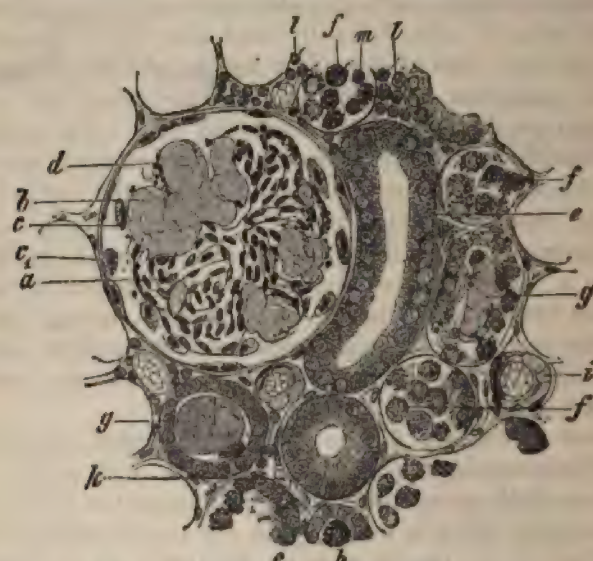


FIG. 208. AMYLOID KIDNEY WITH FATTY DEGENERATION.

(*Treated with Müller's fluid and perosmic acid*: × 300.)

a, normal capillary loop
b, amyloid capillary loop
c, fatty glomerular epithelium
c_1, fatty capsular epithelium'
d, oil-globules lying on the capillaries
e, fatty epithelium *in situ*
f, loosened fatty epithelium
g, hyaline tube casts
h, fatty tube-cast
i, amyloid arteriole
k, amyloid capillary
l, cellular infiltration of the connective tissue
m, round-cells within a urinary tubule

transparent, or firm and waxy. The firmer kinds stain with iodine a somewhat deeper brown than the surrounding structures, but do not usually give the typical amyloid reactions.

In the meshes of the intertubular connective tissue we frequently find cellular infiltrations (*l*), a sign that a certain amount of inflammation accompanies the other changes. Sometimes too there is a certain amount of fibrous hyperplasia and induration.

We have already discussed (Arts. 57–62) the ætiology and the significance of the amyloid degeneration. As to the fatty degeneration which accompanies the amyloid change in the kidney we must assume that it is mainly the effect of the same agencies as the latter, though no doubt the disturbances of the circulation occasioned by the amyloid deposits have something to do with it. The accompanying inflammatory changes too are probably a third effect of the same causes. In support of this view it is to be noted that now and then (NAUWERCK) the presence of bacteria in the vessels of the amyloid kidney can be demonstrated.

References:—Arts. 61, 62; FEHR. *Die amyloide Degeneration* Berne 1867; GRAINGER STEWART, *Bright's diseases* Edinburgh 1871; LITTEN, *Berl. klin. Woch.* 1878; *Med. Times and Gaz.* 2, 1878; DICKINSON, *Diseases of the kidney* II. London 1877; STRAUSS, *Soc. méd. des hôpitaux* 1881; CORNIL, *Practitioner* XXXII. (1882), *Pathologie du rein* Paris 1884.

CHAPTER LXIX.

HÆMATOGENOUS NEPHRITIS.

538. The term **hæmatogenous nephritis** includes all the inflammatory affections of the kidney the exciting cause of which reaches the organ by way of the circulation.

The anatomical condition for the existence of nephritis is the presence of an inflammatory alteration of the blood-vessels. As this is incapable of direct demonstration the evidence of it appears in the presence of an inflammatory exudation.

In glandular organs an inflammatory exudation lodges either in the connective-tissue stroma, or in the lumen of the acini and ducts; in the latter case it mingles with the specific glandular secretion, whose composition is thereby altered.

The kidney is no exception to the rule. But the determination of many points in connection with renal inflammation is rendered difficult by the fact—that the kidney normally contains a large quantity of liquid transuded from the blood-vessels, and thus inflammatory exudations entering the tubular system are frequently not at once distinguishable from non-inflammatory transudations.

Our decision as to whether for example the contents of a Bowman's capsule or a uriniferous tubule are inflammatory or not depends on their composition. Inflammatory exudations are always highly albuminous: they usually contain blood-cells, and often fibrinous coagula. The altered secretion of an inflamed kidney also contains albumen, and generally blood-cells and coagula. If then we are sometimes in doubt as to the nature of a given renal affection it is owing to the fact that a simple degeneration of the glomerular or tubular epithelium, or a transitory disturbance of the circulation, may occasion the escape of albumen from the blood into the urine. If other decisive marks are absent we may fall back on this—that the quantity of albumen in the urine in inflammatory affections of the renal vessels is greater than in simple degeneration or hyperæmia. But after all is said it must be granted that it is impossible to draw an absolutely sharp line between renal inflammations and renal degenerations.

539. Clinical authorities describe three chief types of nephritis.

The first is **acute nephritis**, distinguished by diminution in the

quantity of urine, which is of high specific gravity, contains much albumen, is of acid reaction, and is dark or occasionally smoky or blood-stained in color. The sediment contains white blood-cells, and when the urine is smoky or bloody red blood-cells, also tube-casts which are hyaline or occasionally granular and mingled with red blood-cells or their detritus, epithelial cells from the collecting tubes, turbid swollen and broken-down cells from the convoluted tubules, and sometimes concavo-convex epithelium from the glomeruli.

Scarlatina, diphtheria, croupous pneumonia, relapsing fever, septicæmia, pyæmia, typhoid, endocarditis, and articular rheumatism are frequent causes or concomitants of acute nephritis, though it also arises idiopathically. Anasarca is usually present, but not always, especially in the secondary varieties.

The usual issue of the affection is in recovery, though death may occur from uræmia. Only in rare instances does it pass into chronic indurative nephritis with hypertrophy of the heart and polyuria. More rarely still does it lead to chronic parenchymatous nephritis, and though many cases are of long duration the process does not usually end in a fatal chronic disease, but in ultimate recovery.

The clinical term acute nephritis includes a number of anatomically distinct types of renal inflammation. There is in almost all cases some disorder of the glomeruli, and this may by itself give rise to all the symptoms of acute nephritis; but in many cases the uriniferous tubules or the intertubular stroma or both are also affected, and these changes give rise to corresponding peculiarities in the anatomical aspect of the disease.

The second form recognized by physicians is **chronic parenchymatous nephritis.** Its characters are these:—onset insidious or subacute, and invariably accompanied by anasarca, which may be the first symptom attracting the patient's notice to his condition; urine highly albuminous, slightly diminished in quantity, of a turbid yellow tint, of increased specific gravity, and usually free from blood, though hæmorrhagic varieties occur; in the sediment numerous tube-casts of various sizes, white blood-cells, fatty epithelial cells, granular and fatty detritus, and fat-granule cells. Red blood-cells are usually few or absent, being abundant only in the hæmorrhagic forms.

Recovery is rare. As a rule after the disease has lasted for months or years death ensues from increasing dropsy, cerebral œdema, pleurisy, pericarditis, uræmia, or other cause. Sometimes however the aspect of the case changes: cardiac hypertrophy and rise of the arterial blood-pressure cause the flow of urine to increase, its specific gravity and proportion of albumen diminish, the dropsy disappears, and the case presents the features of renal cirrhosis.

The third form is **renal cirrhosis** or **indurative nephritis.** It is characterized by the following features:—increased flow of pale slightly

albuminous urine of low specific gravity; sediment containing few formed elements, pale hyaline casts, white blood-cells, and occasionally a few red blood-cells; anasarca absent; the heart hypertrophied; the fundus of the eye affected by a special form of neuro-retinitis. The onset is usually very gradual, and the first symptoms of the malady are disorders of digestion or of vision, palpitation, cardiac distress, etc. After a duration of years death ensues from such causes as cardiac failure, dropsy, cerebral hæmorrhage, uræmia, purulent inflammations of serous membranes, etc.

Rarely are the essential symptoms of renal cirrhosis presented by a case commencing as an acute nephritis; such cases when they occur are usually marked by their rapid course.

Chronic parenchymatous nephritis is characterized anatomically by great degeneration of the renal epithelium: renal cirrhosis by marked changes in the connective tissue of the vascular system. The two forms are thus distinguishable anatomically as well as clinically, and the pathological anatomist may therefore accept the clinical classification. It is however to be kept in mind that the two forms are by no means antithetic; the distinction is rather one of degree than of kind. In the former affection the connective-tissue elements undergo some morbid change, in the latter there is always some epithelial degeneration. There are in fact numerous intermediate and transitional forms partaking of the characters of both.

The attempt has often been made to interpret the several forms of nephritis as stages of a single morbid process. But apart from the fact that acute nephritis does not usually pass into any of the chronic forms, there is this insuperable objection—that a given condition of the kidney in chronic nephritis may have been arrived at in several very different ways. There is no doubt at least that the mode of beginning of the disease differs in different cases. There is as little ground for the view that all forms of nephritis begin with glomerular changes, as that they all begin with epithelial degeneration or interstitial infiltration. And if the mode of beginning varies so also does the further course of the disease; we are in fact unable to say of a given advanced renal affection either how it began or what stages it has passed through. We can in general as little forecast how a given acute inflammation of the kidney would have terminated had the patient lived. We must therefore content ourselves with describing as accurately as possible the several forms that offer themselves for examination, and suggesting the possible ways in which these forms may have arisen.

The modern investigations of the affections included under the term nephritis begin with the observation of BRIGHT (*Report of medical cases selected with a view of illustrating the symptoms and cure of diseases by a reference to morbid anatomy* I. London 1827) that certain cases of dropsy depended on disease of the kidney, and were distinguished by albuminous urine. BRIGHT himself de-

scribed various forms of renal disease leading to albuminuria. These affections have since been included under the term **Bright's disease** (*Morbus Brightii*); but the term has been variously applied by various authors—some including under it all renal affections associated with albuminuria, others excluding the simple degenerations and disorders of circulation and including only the inflammatory affections.

ROKITANSKY (*Handb. d. path. Anat.* II. 1842) distinguished eight forms. FRERICHS (*Die Bright'sche Nierenkrankheit* Brunswick 1851) regarded the different forms merely as different stages of one and the same process. This process, he held, began with hyperæmia, passed on to exudation and parenchymatous degeneration, and ultimately issued in atrophy and contraction.

The works of BRIGHT and FRERICHS have given rise to a vast number of memoirs of which the following may be particularly mentioned:—CHRISTISON, *On granular degeneration of the kidnies* Edinburgh 1839; RAYER, *Traité des maladies des reins* Paris 1840; WILKS, *Cases of Bright's disease. Guy's Hosp. Reports* VIII. (1853); VIRCHOW, *Virch. Arch.* vol. 4; JOHNSON, *Diseases of the kidney* London 1852; *Lectures on Bright's disease* London 1873; GULL and SUTTON, *Med. chir. Trans.* IV. (1872); BEER, *Die Bindesubstanz d. menschl. Niere* Berlin 1859; FÖRSTER, *Hand. d. path. Anat.* 1863; DICKINSON, *Med. chir. Trans.* XLIII., XLIV. (1860–61), *Pathology of Albuminuria* London 1868, *Renal and urinary affections* London 1877–85; TRAUBE, *Gesamm. Abhandl.* II. (1871); KLEBS, *Handb. d. path. Anat.* Berlin 1870; GRAINGER STEWART, *Bright's diseases of the kidney* Edinburgh 1871; RINDFLEISCH, *Path. Hist.* II. (New Syd. Soc.) London 1873, BARTELS, *Ziemssen's Cyclop.* XV.; KELSCH, *Arch. de physiol.* 1874; GALABIN, *Bright's disease and changes in the vascular system* London 1874; MAHOMED, *Med. chir. Trans.* LVII. (1874), *Lancet* 1, 1879; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1886; LECORCHÉ, *Traite des maladies des reins* Paris 1875; CHARCOT, *Leçons sur les maladies du foie et des Reins* Paris 1877; BUHL, *Mitth. a. d. path. Inst. zu München* Stuttgart 1878; AUFRECHT, *Die diffuse Nephritis* Berlin 1879, *Cent. f. med. Wiss.* 47, 1882 and *Deutsch. Arch. f. klin. Med.* XXXII.; WEIGERT, *Sammlung klin. Vorträge* 162, 163 (1879); RIBBERT, *Nephritis u. Albuminurie* Bonn 1881; HORTOLÈS, *Etude du processus histologique des nephrites* Paris 1881; BAMBERGER, *Sammlung klin. Vorträge* 173 (1879); WAGNER, *Deutsch. Arch. f. klin. Med.* XXV., XXVII., XXXVIII., *Ziemssen's Handbuch* (3d German edition) IX. Leipzig 1882; ROSENSTEIN, *Path. u. Therap. d. Nierenkrankh.* 1870; FISCHL and SCHÜTZ, *Prag. Zeitschr. f. Heilk.* III. (1882); LETZERICH, *Virch. Arch.* vol. 55; LANGHANS, *ibid.* vol. 76; THOMA, *ibid.* vol. 71; SENATOR, *ibid.* vol. 73; GRAWITZ and ISRAEL, *ibid.* vol. 73; POSNER, *ibid.* vol. 79; SAMUEL, *ibid.* vol. 73; EWALD, *ibid.* vol. 71; PLATEN, *ibid.* vol. 71; EBERTH, *Zur Kenntniss bacter. Mycosen* Leipzig 1872; HOFMEIER, *Zeit. f. Geburtshilfe* III.; ZIEGLER, *Deutsch. Arch. f. klin. Med.* XXV.; LITTEN, *Charité-Annalen* IV., *Berl. klin. Woch.* 1873; WEISSGERBER and PERLS, *Arch. f. exp. Path.* VI.; LANCEREAUX, *Dict. encyc.* Paris 1881; LEYDEN, *Zeitschr. f. klin. Med.* III.; Discussion, *Trans. internat. med. congress* II. London 1881; Discussion, *Congress f. innere Medicin* Wiesbaden 1882; FRIEDLÄNDER, *Arch. f. Anat. u. Physiol.* 1881, *Fortschritte d. Med.* I. (1883); BRAULT, *Des formes anatomo-path. du mal de Bright*, *Arch. générales de méd.* 1882; CORNIL and BRAULT, *Journ. de l'anat.* XIX. (1883), *Practitioner* XXVII., XXVIII., XXXII. (1881–84); DUNIN, *Virch. Arch.* vol. 93; FISCHL, *Beiträge z. Histol. d. Scharlachniere, Zeitschr. f. Heilk.* IV.; Discussion on Albuminuria, *Glasg. Med. Journ.* 1884; BIERMER, *Breslau ärztl. Zeitschr.* 1, 1882; SEMMOLA, *Revue médicale française* 1883; NAUWERCK, *Beiträge zur Kenntniss des Morbus Brightii* Jena 1884 (with a critical account of various theories); SENATOR, *Albuminuria in health and disease* (New Syd. Soc.) London 1884; ROBERTS, *Urinary*

and renal diseases London 1885; HOLSTI, *D. Arch. f. klin. Med.* XXXVIII. (1886) SAUNDBY and GREENFIELD, *Trans. Path. Soc.* XXXI.

KLEBS excludes the non-inflammatory renal degenerations from the category of Bright's disease, and identifies the latter with primary interstitial nephritis; the associated changes in the epithelium he regards as secondary. JOHNSON regards the presence or absence of epithelial degeneration and desquamation as an essential feature, and treats of nephritis as desquamative or non-desquamative, each form having its subordinate varieties. GRAINGER STEWART speaks of 'Bright's diseases,' and distinguishes three forms—the inflammatory form, the amyloid form, and the cirrhotic or contracting form. Of the first he describes three stages—that of inflammatory exudation, of fatty change, and of atrophy. VIRCHOW (*Cellular Pathology* London 1860) also distinguishes three forms—parenchymatous nephritis, indurative interstitial nephritis, and amyloid degeneration. BARTELS divides Bright's disease into—acute parenchymatous, chronic parenchymatous, and interstitial nephritis. LECORCHÉ distinguishes only a parenchymatous and an interstitial form. CHARCOT on grounds partly clinical, partly anatomical, makes three—the first characterized clinically by its rapid course, scanty urine with abundant albumen, and dropsy, and anatomically by its large white kidney; the second by its chronic course, abundant urine with little albumen, absent or slight dropsy, and contracted kidney; the third form is the amyloid degeneration. WEIGERT divides Bright's disease into parenchymatous degenerations and true nephritis; the former are all acute affections; the chronic forms are but modifications of one and the same process: he deems it impossible to distinguish interstitial from parenchymatous forms, inasmuch as all forms begin with degeneration and loss of epithelium, and then pass into the stage of reactive interstitial inflammation. DICKINSON makes three classes—tubal nephritis (acute and chronic), granular degeneration with hyperplasia and contraction of the stroma, and depurative disease (or amyloid degeneration). AUFRECHT speaks of an acute, a subacute, and a chronic nephritis, and maintains that the primary change is an affection of the tubular epithelium, the vessels and the fibrous structures being affected secondarily: he describes amyloid disease as a nephritis. WAGNER considers that Bright's disease is a clinical term, implying a disease in which the urine exhibits certain morbid changes: he treats it under the four heads of (1) acute Bright's disease, (2) chronic Bright's disease, (3) contracted kidney, (4) amyloid kidney. LEYDEN defines the term Bright's disease from the clinical or physiological point of view (*Congress f. innere Med.* Wiesbaden 1882) as an affection characterized by albuminuria and dropsy, including in the term renal degenerations, pyelonephritis, amyloid change, etc. ROSENSTEIN (*ibidem*) thinks on the other hand that the term must be defined according not to clinical but to pathological and anatomical characters. CORNIL uses the term albuminous nephritis as equivalent to Bright's disease and treats the various forms under the heads of acute nephritis, parenchymatous or epithelial nephritis, and interstitial nephritis.

The above summary shows how widely authorities differ as to the content of the term Bright's disease, and as to the anatomy and pathogenesis of nephritis. We might easily carry our references further and so bring out still greater differences. This is true not only of the older authorities, but even of the most recent, the latest discussions on the subject showing clearly that on the basis of our present knowledge no reconciliation of the conflicting views is possible.

This being the case the author has thought it best in dealing with the pathological anatomy of the nephritic process to refer as little as possible to the existing literature of the subject, and to be guided mainly by the results of his own investigations. This he has done with less hesitation inasmuch as for some years he has given considerable attention to the subject and has collected an extensive

series of observations on it. During the last two or three years he has had the further advantage of watching the results of a research on nephritis carried out in his presence by Dr. NAUWERCK. His work has thrown much light on the subject, and some of the figures hereafter given are taken from his admirable preparations. The experimental researches on nephritis made by GRAWITZ and ISRAEL, PONFICK, LASSAR, MARCHAND, AUFRECHT, BUCHWALD, LITTEN, and others have but slight bearing on the questions raised by the phenomena of nephritis in man. The varieties of renal degeneration set up by the injection or administration of various chemical irritants or by interruptions of the blood-supply, etc. have but distant relation to nephritis proper, and admit of useful comparison with the human affections exactly corresponding to them and with no others. Still less have the degenerations of the kidney induced by ligature of the ureter to teach us concerning the textural changes in human hæmatogenous nephritis. For this latter we must in the first place look to a careful anatomical investigation of the diseased human kidney.

As to the exact significance to be attached to the term Bright's disease we must leave clinical experts to decide. It is essentially a clinical term, and the pathological anatomist may for the present dispense with it.

Acute Nephritis.

540. **Acute glomerulo-nephritis.** The simplest form of acute nephritis is that in which the inflammatory changes are in the main confined to the glomeruli, the intertubular vessels being but slightly affected.

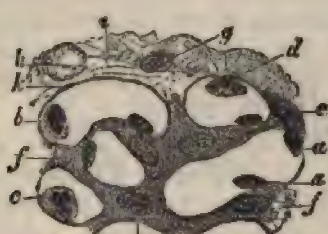


FIG 209. SECTION THROUGH GLOMERULAR CAPILLARIES IN ACUTE NEPHRITIS FOLLOWING DIPHTHERIA: AFTER *NAUWERCK.*

(The glomerulus lies near the surface of the kidney: section hardened in alcohol, stained with alum-carmine and eosin, and mounted in Canada Balsam: × 450.)

a, nucleus in capillary-wall
b, swollen and loosened endothelial cell
c d, endothelial cells with multiple nuclei
e, glomerular epithelium
f, disintegrating glomerular epithelium
g, nucleus of a detached epithelial cell
h, vesicular (degenerate) epithelial cell
i, coagulated albumen
k, denuded capillary wall

The glomeruli themselves often show no marked histological change; the presence of an albuminous exudation, which coagulates by alcohol or by heat and forms a crescentic areola around the glomerular vessels, being sometimes the only evidence that the vessels have been altered. Other glomeruli may be somewhat swollen, or partially denuded of epithelium (Fig. 209 *g h*; Fig. 213 *e*, Art. 544). In more severe cases some of the capillary loops are entirely denuded (Fig. 207 d, Art. 535),

Fig. 209 *k*; Fig. 212 *b*, Art. 543), and the vessels look pale, denucleated, and necrotic; or they are transformed into homogeneous spherules with few or many nuclei, larger than the normal glomeruli and impermeable by the blood or by artificial injections. According to FRIEDLÄNDER the latter is the form most frequent in post-scarlatinal nephritis, and it may extend over a great part of the kidney. It would appear to be due to a hyaline swelling (Art. 63) of the vessel-walls themselves.

Some of the capillaries appear to contain an excess of white blood-corpuscles and it is possible that this may occasionally give rise to thrombosis (RIBBERT). According to LANGHANS and NAUWERCK the endothelial cells of the capillary loops become swollen (Fig. 209 *a*), proliferous, loosened (*b*), and degenerate (*d*), the epithelial cells of the glomeruli (*h k*) also undergoing desquamation. Hæmorrhagic exudation is very common, the capsule of the glomerulus then becoming tightly distended with blood (Fig. 212 *f*, Art. 544).

The tubular epithelium may be altogether unaltered. In other instances single cells may appear degenerate, turbid, fatty, or necrotic, or they may be loosened and disintegrated. Hyaline casts occupy the lumen of some of the tubules.

The intertubular connective tissue is in general entirely unaffected; now and then it appears somewhat swollen from inflammatory œdema, or contains a few scattered patches of cellular infiltration.

The naked-eye appearance of the kidney is not usually altered to any sensible extent. Only when there is great hyaline thickening of the glomerular capillaries do the glomeruli become noticeable by their paleness and increased size (FRIEDLÄNDER).

Glomerulo-nephritis is not a specific disease, as it can be produced by a variety of causes. According to KLEBS, FRIEDLÄNDER, CORNIL, KLEIN, etc. it is specially apt to follow upon scarlatina. It may also accompany pyæmia, septicæmia, diphtheria, relapsing fever, erysipelas, carbuncle, etc., or arise idiopathically, that is without any antecedent infective disease. It obviously is due to the action of deleterious substances reaching the glomerular vessels by way of the circulation, and damaging the vessels in the process of excretion through their walls. It thus stands ætiologically in close relation with the forms of degeneration described in Arts. 534, 535, and indeed it is difficult or impossible to draw a sharp line separating the histological appearances in the two groups.

Glomerulo-nephritis may cause death by suppression of the urinary secretion. In other cases it issues in recovery, or in chronic change.

References:—KLEBS, *Handb. d. path. Anat.* I.; KELSCH, *Arch. de physiologie* 1874; KLEIN, *Reports to Med. Off. of Privy Council* 1876; LANGHANS, *Virch. Arch.* vols. 76, 99; HORTOLÈS, *Etude d. proc. histol. des néphrites* Paris 1881; LEECH, *Brit. Med. Journ.* 1, 1881; GREENFIELD, *Atlas of Pathology* (New Syd. Soc.) London 1879; RIBBERT, *Nephritis u. Albuminurie* Bonn 1881; COHNHEIM, *Allg. Path.*

II. 1882; FRIEDLÄNDER, *Fortschritte d. Med.* I (1883); CORNIL, *Practitioner* XXVIII, XXXII. (1882–84); CORNIL and BRAULT, *Pathologie du rein* Paris 1884; B. C. WALLER, *Journ. of Anat. and Physiol.* XIV. 1879; NAUWERCK, *Beitr. z. Kennt. d. Morb. Brightii* Jena 1884.

541. **Acute diffuse nephritis** with sero-fibrinous exudation, or as we may call it acute inflammatory œdema of the kidney, gives rise to more or less swelling of the organ, in some cases so extreme that it attains a length of 22 to 25 centimetres. The capsule is easily stripped off, the surface smooth, the tint gray or grayish-red speckled with yellowish-red. On section the cortex and medulla appear swollen and sodden, usually pale-gray or grayish-yellow, and occasionally streaked or speckled with red. The whole organ is soft, especially so when the swelling is great.

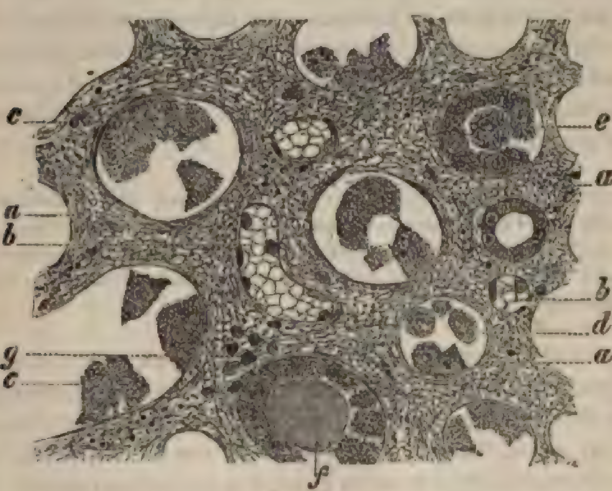


FIG. 210. DIFFUSE NEPHRITIS WITH SERO-FIBRINOUS EXUDATION.

(*Section treated with perosmic acid and mounted in glycerine*; × 350.)

a, stroma much thickened and beset with fibrinous threads and granules and with oil-globules
b, capillaries
c, epithelium of the convoluted tubules, partly turbid, partly fatty and desquamating
d, shed epithelium in a Henle's loop
e, granular and fatty detritus in a Henle's loop, whose epithelium is turbid but remains *in situ*
f, hyaline cast
g, extravasated leucytes

The swelling is due mainly to the accumulation of liquid in the intertubular connective tissue of the cortex (Fig. 210), and to some extent of the medulla.

The stroma is greatly thickened and contains a liquid which in recent preparations, more commonly however in hardened ones, is mingled with threads and granules of fibrin (*a*). The vessels may be compressed

by the liquid, but sometimes at least in places appear distended with blood (*b*).

The exudation contains few cells, though it is not unusual to find scattered patches of cellular infiltration (*g*). When the condition is no longer quite recent the intertubular exudation contains oil-globules.

The glomeruli are for the most part not perceptibly altered, though when treated with alcohol traces of coagulable exudation can be made out within their capsules. In some of the glomeruli moreover there is slight swelling and desquamation of the epithelium.

The tubular epithelium of the cortex and medulla is everywhere more or less swollen and loosened (*c*), in many places it is actually detached (*d*). Sooner or later fatty degeneration and disintegration of the epithelium becomes apparent.

The tubules are at first empty, but presently they are filled with hyaline casts (*f*), or with granular and fatty epithelial detritus (*e*).

The slighter forms of inflammatory œdema accompany the various infective diseases, such as typhoid fever, and give rise to some swelling and considerable dropsical saturation of the kidney. The more intense forms are seldom met with: they are most common in affections of the nature of pyæmia.

The drawing in Fig. 210 was made from the kidney of a patient who died on the tenth day of an acute febrile attack. The disorder was obviously of an infective nature, for the renal inflammation was accompanied by enormous swelling of the spleen, with purulent inflammation in the mediastinum, and later on with purulent pleurisy.

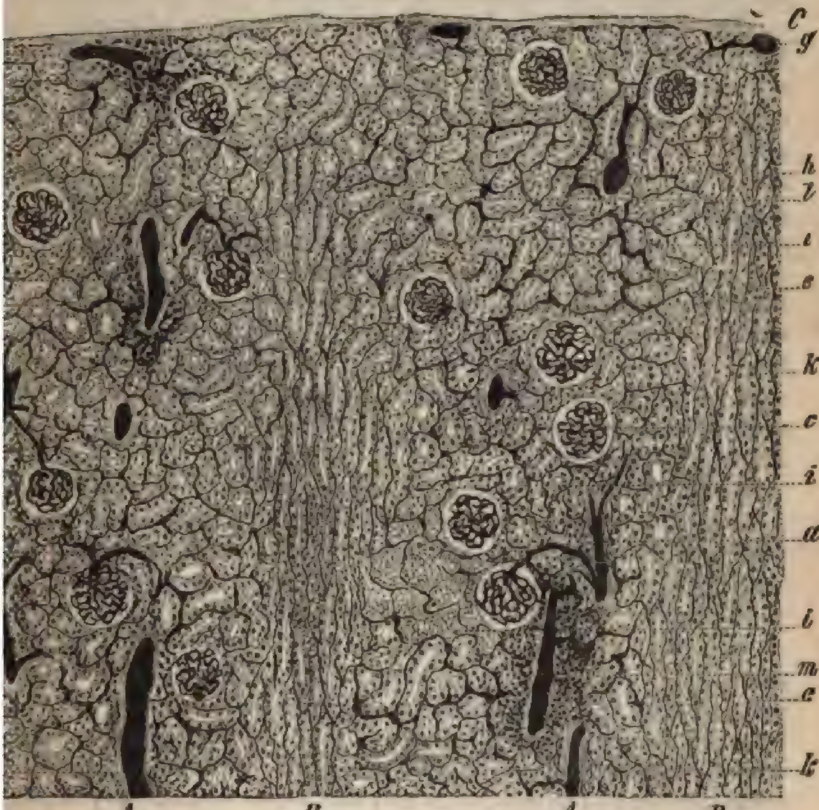
542. **Acute disseminated interstitial nephritis** is the most common form of acute renal inflammation. The kidney is swollen but little or not at all, and at first the section shows no discoloration whatsoever. Only when the interstitial changes are accompanied by marked degenerative changes do spots and patches of gray or (in fatty degeneration) white make their appearance. Hæmorrhage is frequently an early symptom, and gives rise to small punctiform dark-red spots.

The diagnosis of this form of nephritis can be made with certainty only by means of the microscope.

The cellular infiltration (Fig. 211 *m*) first makes its appearance around the stellate veins (*g*) and the interlobular veins (*h*), and is usually so marked that in stained sections the affected patches can be seen under very low magnifying powers. These patches are usually most abundant in the outer zone of the cortex, and in the boundary zone between the cortex and medulla; the middle parts of the cortex being seldom much affected. The glomeruli which lie within the region of the inflamed veins may be surrounded with infiltrated cells, the latter often accumulating in a dense mass round the glomerular capsule. The connective tissue not lying within this region may be entirely unaffected, though

s occur in which other capillary regions, especially those around the ieruli (Fig. 213, Art. 544 and Fig. 212, Art. 543), show signs of e or less extensive cellular infiltration.

The tubular epithelium may be altogether normal. Even in the re of the inflamed region the cells occasionally remain unchanged or iost become a little cloudy, their form being retained and their ei continuing to stain well. NAUWERCK has observed this condition ie nephritis accompanying infective pneumonia. In other cases the



1. OUTER HALF OF THE CORTEX IN RECENT ACUTE DISSEMINATED (INTERSTITIAL) NEPHRITIS.
(*Injected with Prussian blue and stained with alum-carmine* : × 32.)

A, labyrinth — *B*, medullary rays — *C*, capsule

rlobular artery — *h*, interlobular veins
afferens — *i*, convoluted tubules
nerulus — *k*, straight tubules (Henle's loops and collecting tubes)
efferens — *l*, degenerate convoluted tubules
llaries of the medullary rays — *m*, cellular infiltration around the veins
llaries of the labyrinth
late veins

elium is in parts more obviously affected by the inflammatory pro- and cloudy swelling with a tendency to necrosis is observed, espe-

cially in the convoluted tubules (Fig. 211 *l*). According to NAUWERCK this occurs chiefly in cases of diphtheria. The affected epithelial cells sooner or later lose their nuclei.

The degeneration and necrosis of the epithelium may either be confined to the inflamed region, or may extend beyond it. It is worthy of remark that in certain conditions the epithelium in the inflamed region may be little if at all altered, while in other parts epithelial necrosis has set in. Frequently we find that the cells of the collecting tubes are the most altered, being turbid or disintegrated into granular detritus.

The glomeruli themselves are as a rule but little affected, except in those cases which tend to issue in suppuration (Art. 543). Sometimes a few of them are partially denuded of their epithelium. Cases also occur in which at an early stage of the inflammation the epithelia of some of the capillary loops become necrosed and denucleated (Fig. 207, Art. 535), and fall away from their attachments. The capsules of some glomeruli also contain an exudation which coagulates with alcohol into a granular mass, and contains the desquamated and degenerate glomerular epithelium in the form of transparent vesicular spherules. When hæmorrhage takes place, many of the capsules contain blood, which closely surrounds the vascular loops (Fig. 213, Art. 544) and passes down into the corresponding tubules. Varieties of nephritis are met with in which these hæmorrhages are from the outset numerous and abundant, so much so that they may throw the interstitial changes quite into the background.

In the lumen of the tubules, especially in the loops of Henle, are formed hyaline casts, sometimes enclosing a few scattered nuclei. The tubules bordering on the patches of cellular infiltration also contain leucocytes, which have traversed the membrana propria and lie either within the tubules or in their secreting epithelium.

Disseminated interstitial nephritis may coexist with inflammatory œdema. The kidney is then more or less swollen, and mottled with red and gray. This condition is met with in connection with various infective diseases, more especially in pneumonia and erysipelas (NAUWERCK, MOMMSEN); and also in scarlatina, diphtheria, pyæmia, and relapsing fever (PONFICK). It may also occur without any antecedent general infection of the system. It issues in recovery, or in localized induration and atrophy, or in suppuration.

RIBBERT maintains that every interstitial nephritis begins in an inflammatory change of the glomeruli. WEIGERT thinks all forms of nephritis begin in epithelial degeneration. Both views are one-sided and apply only to a limited number of cases; they relegate the essential part of the process to a secondary place. Nephritis may begin in many different ways, and no single scheme can be laid down to which all cases shall conform.

References on nephritis following pneumonia :—WAGNER, *Deut. Arch. f. klin. Med.* XXV.; MOMMSEN, *Deutsch. med. Woch.* 1879; NAUWERCK, *loc. cit.*; JÜRGEN-

SEN. *Croupöse Pneumonie* Tübingen 1883: FRIEDLÄNDER. *Fortschritte d. Med.* II. 1884; DICKINSON, *Renal and urinary affections* III. London 1885.

References on nephritis after diphtheria, scarlatina, etc.:—BOUCHARD, *Rev. de méd.* 1881; CAPITAIN and CHARRIN, *ibid.*; GAUCHER, *Lancet* 1, 1881; CORNIL, *Journ. de l'anat.* 1879, *Practitioner* XXVIII., XXXII. (1882–84); EBERTH, *Virch. Arch.* vol. 57, *Zur Kenntniss bacter. Mycosen* Leipzig 1872; JACOBI, *Gerhardt's Handb. d. Kinderkrankh.* II.; KANNENBERG, *Zeitschr. f. klin. Med.* I.; KLEBS, *Handb. d. path. Anat.*; KLEIN, *Trans. Path. Soc.* XXVIII. (1877); LÉPINE, *Revue mensuelle* 1880; LETZERICH, *Virch. Arch.* vols. 47, 52, 55, 61; LEYDEN, *Zeitsch. f. klin. Med.* III.; LITTEN, *ibid.* IV.; MARKWALD, *Ueber die Nierenaffection bei acuten Infectionskrankh.* In. Diss. Königsberg 1878; OERTEL, *Ziemssen's Cyclop.* II.; SENATOR, *Virch. Arch.* vol. 56, *Die Albuminurie im gesund. u. krank. Zustande* Berlin 1882, trans. by SMITH (New Syd. Soc.) London 1884; THOMAS, *Gerhardt's Handb. d. Kinderkrankh.* IV.; UNRUH, *Jahrb. f. Heilk.* XVII. (1881); P. FÜRBRINGER, *Virch. Arch.* vol. 91; NAUWERCK, *Die Nephritis* Jena 1883; FISCHL, *Beiträge z. Histologie d. Scharlachniere*, *Zeitsch. f. Heilk.* 1883; LEICHTENSTERN, *Deutsche med. Woch.* 1881; BABES, *Arch. de physiol* II. (1883); FRIEDLÄNDER, *Fortschritte d. Med.* I. (1883); Art. 540.

ATKINSON (*Amer. Journ. med. sciences* 1884) gives a good account (with references) of nephritis from malarial poisoning.

543. **Disseminated suppurative nephritis.** When a simple disseminated nephritis issues in suppuration, there are formed in various parts of the kidney, especially in the cortex but not infrequently in the medulla also, a number of rounded or linear patches of whitish pus-like matter usually surrounded by a zone of hyperæmia. In other respects the kidney may be almost normal, though there is frequently a certain amount of swelling (from inflammatory œdema) and some gray and red mottling (from disorder of the circulation).

The smallest patches (not larger than a millet-seed) are due to a steadily increasing extravasation of leucocytes, which accumulate either round the venules or round the capsules of the glomeruli.

Suppurative inflammation of the kidney is no doubt in general a result of bacterial invasion. When the micro-organisms settle within the capillary loops of the glomeruli (Fig. 212 *a*) they first block up the lumina of the vessels, then induce necrosis of the glomerular epithelium (*b*), and finally necrosis of the glomerulus itself. An inflammatory reaction is thereupon set up around the glomerulus, the first effect of which is an accumulation of extravasated leucocytes in the surrounding connective tissue (*d*). There is also usually a certain amount of exudation from the intertubular venules (*f*). The epithelium within the affected region as a rule degenerates rapidly (*g h*). Part breaks up into granular detritus, part becomes necrotic and denucleated, and desquamates. The extravasated leucocytes penetrate the tubules (*i*), and in a short time the entire region is thickly infiltrated with them. By and by not only the epithelium but the connective tissue breaks down, and the infiltration becomes an **abscess**. The size of the abscess depends of course on the extent of the infiltration.

This form of inflammation may result in the breaking down of a large part or even the whole of the kidney, so that at length nothing remains but a sac filled with pus. The latter is however not a common result of the affection now considered; it occurs much more frequently as a sequel of pyelonephritis (Art. 554).

Wide-spread suppuration of the renal tissue gives rise to catarrhal, purulent, or even diphtheritic inflammation of the pelvis of the kidney: and not infrequently abscesses are formed in the surrounding subperitoneal tissue (**perinephritic abscess**).

Suppurative nephritis (not due to pyelonephritis) occurs most frequently in connection with ulcerative endocarditis and with traumatic pyæmia. It may however be associated with a great variety of diseases, such for instance as dysentery, ulcerative phthisis, and actinomycosis (ISRAEL, *Virch. Arch.* vol. 74). The abscesses are usually punctiform or miliary; large abscesses are rare.

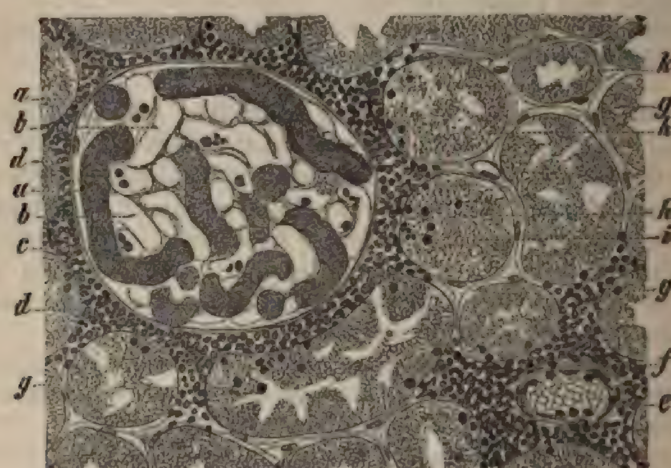


FIG. 212. DISSEMINATED SUPPURATIVE NEPHRITIS.

(*Section stained with gentian-violet and mounted in Canada Balsam:* × 200.)

a, capillary loop filled with micrococci
b, empty denucleated capillary
c, leucocytes in the capillaries
d, cellular infiltration around the capsule
e, venule
f, cellular infiltration around the venule
g, convoluted tubule, with epithelium partly cloudy, partly denucleated and degenerate
h, convoluted tubule with granular detritus
i, leucocytes within the tubules
k, limb of Henle's loop

Suppurative nephritis is not infrequently combined with embolic obstruction of the renal arteries, leading to the formation of infarcts.

According to LITTEN (*Zeitschr. f. klin. Med.* IV.) there are some forms of acute nephritis in which large numbers of micrococci are diffused throughout the whole of the kidney, filling up many of the tubules and Bowman's capsules. AUFRECHT reports similar cases (*Pathologische Mittheilungen* I. 1881. LETZERICH (*loc. cit.*) affirms that in diphtheria masses of micrococci may accumulate to such an extent in the circulatory and secretory channels that the urinary function is gravely interfered with.

ZIEGLER has never been able to discover such extensive accumulations of bacteria in the kidney, even in cases of diphtheria. The suspicion arises that some other appearance has been mistaken for colonies of micrococci. Treatment of the sections with alkalies and alcohol is not sufficient to determine with certainty the presence of these organisms.

BABES (*Arch. de physiol.* II. 1883) has recently described various forms of bacteria discovered by him in the renal blood-vessels in certain forms of nephritis accompanying pyæmic and septicæmic infection, scarlatina, articular rheumatism, yellow fever, etc. In connection with the latter he found chaplets of two to six diplococci, and suggests that they may be the exciting cause of the disease. STEVEN (*Glasgow Med. Journ.* 1884) discusses the suppurative affections of the kidney in a clear and able manner.

Chronic Parenchymatous Nephritis.

544. The inflammations of the kidney comprehended under the term **chronic parenchymatous nephritis** are all characterized by persistent inflammatory exudation from the blood-vessels into the renal tissue, accompanied by marked alteration of the epithelial structures. The persistent exudation takes place partly from the glomeruli and partly from the intertubular capillaries and venules.

The intertubular exudation saturates the renal tissues with inflammatory lymph, varying in quantity at different stages of the process and in different cases.

This inflammatory œdema is always accompanied by a more or less extensive cellular infiltration (Fig. 213 *q r*), which is often remarkably dense around the subcortical and interlobular venules (*q*), often also well-marked in the neighborhood of the intertubular capillaries (*r*) and here and there in exceptional amount round a few of the glomeruli. The extravasated leucocytes (*q*) and the liquid exudation may penetrate directly into the tubules, and the leucocytes gathered around the Bowman's capsules may in like manner penetrate them. Intertubular venous hæmorrhages are occasionally observed, and when the tubules are at the same time ruptured blood may enter these directly (NAUWERCK).

The vessels of certain of the glomeruli permit the escape of albuminous urine, which even during life may coagulate into a granular or homogeneous mass within the capsules. More commonly however coagulation takes place only within the tubules (especially in the loops of Henle), giving rise to the familiar hyaline casts or cylinders.

The glomerular capillaries frequently permit the escape of white (*e*) and red (*f*) blood-cells. The former often accumulate in great quantity in the capillary loops (*b*) before escaping, but they do not usually escape in large numbers into the lumen of the capsule.

Comparatively few of the red blood-cells (*e*) escape into the lumen of the capsules, though not infrequently larger extravasations are observed in which the capsules and their tubules appear widely distended with blood (*f p*).

In many cases the glomerular epithelium looks perfectly normal, but it is more common to find it somewhat swollen, the individual cells standing out clearly from the contours of the capillaries. Multiplication and

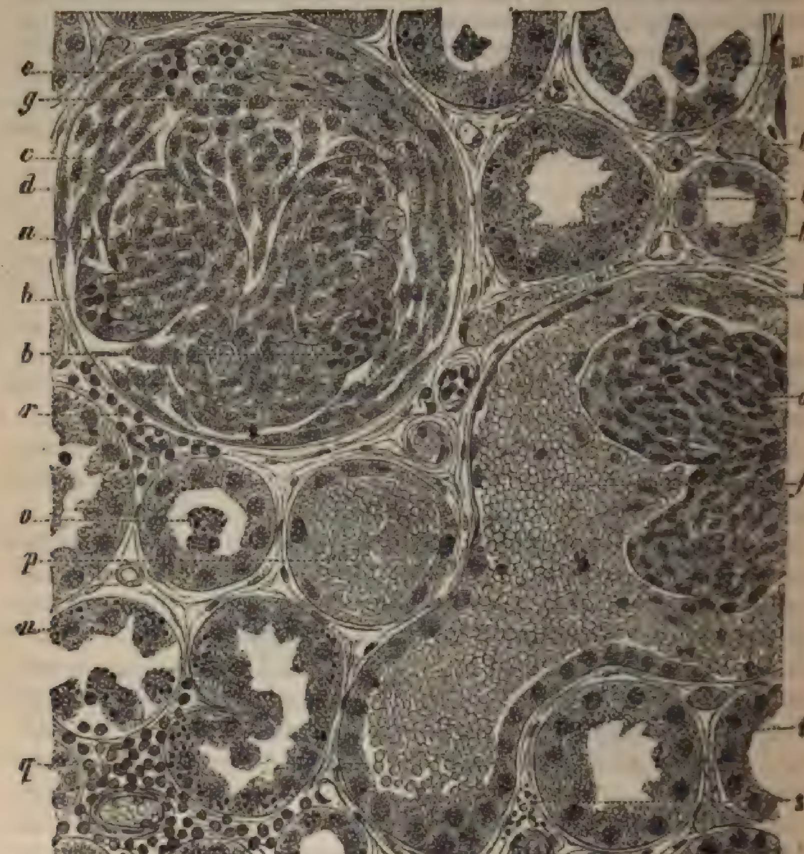


FIG. 213. CHRONIC HÆMORRHAGIC (PARENCHYMATOUS) NEPHRITIS.

(Section hardened in Müller's fluid, stained with alum-carmine, and mounted in Canada balsam: the fatty change represented is taken from another preparation treated with perosmic acid: × 300.)

- *a*, normal capillary loop
- *b*, capillary filled with white blood-cells
- *c*, desquamated glomerular epithelium
- *d*, capsular epithelium
- *e*, exudation consisting of red and white blood-cells and granular matter
- *f*, hæmorrhage into a capsule and tubule
- *g*, granular stratified exudation, containing nuclei of desquamated glomerular epithelium
- *h*, disintegrated blood containing desquamated glomerular epithelium
- *i*, convoluted tubule
- *k*, limb of Henle's loop
- *l*, tubule with pigmented and fatty epithelium
- *m*, pigmented and desquamated epithelium
- *n*, fatty cells, some of them desquamated
- *o*, loose fatty epithelial cells in the lumen of a normal tubule
- *p*, tubule filled with blood
- *q r*, cellular infiltration around venules and capillaries
- *s*, pigment-granules in stroma
- *t*, capillaries filled with blood

desquamation usually set in, and epithelial cells are seen in greater or less numbers lying loose within the capsules (*c*). These may be washed out unchanged into the tubules, but at times they accumulate in quantity within the capsule, surrounding the glomerular vessels in successive strata (*c*) and separating or compressing the loops by their intrusion. Frequently too the cells break down or dissolve in the liquid escaping from the glomerular vessels, and homogeneous or granular coagula (*g h*) are thus formed, which more or less completely ensheath the glomerulus. The nuclei enclosed in these coagula often persist for a long time, and occasionally give them the appearance of intracapsular new-formations of connective tissue.

In addition to the swelling and desquamation of the epithelium we often remark a certain amount of fatty change, which gives the cells the look of being powdered or sprinkled with minute globules.

The glomerular capillaries appear for the most part unaltered, though all the changes described in Art. 540 may occasionally be observed.

The capsular epithelium (*d*) is as a rule far less altered than the glomerular, though it too may in certain cases become swollen, break up, and desquamate. It may also undergo fatty degeneration.

The tubular epithelium always shows more or less marked signs of cloudy swelling, fatty degeneration, desquamation, and disintegration. The most striking of these changes, the fatty degeneration (*l m n*), is distinguished by the presence of droplets and globules of oil within the cells, varying in size and number according to the degree of degeneration. The fatty cells (*m o*) are the most apt to be shed, though this happens also in the case of the swollen and cloudy cells. These desquamated cells dissolve *in situ* or are carried into remoter parts of the tubules, where they may coalesce into hyaline cylinders.

The degenerative changes affect chiefly the convoluted tubules, though they are not entirely absent in the loops and collecting tubes. In the latter especially there may be very marked desquamation of the epithelium.

When considerable hæmorrhages have taken place in the glomeruli the corresponding tubules are distended with blood, their epithelium appearing compressed and flattened (*p*). The blood presently disintegrates, forming granules and flakes of pigment: these are usually taken up by the epithelial cells (*l m*), part also appearing in the fibrous stroma (*s*) whither they are carried by the absorbents (Art. 530).

In many cases it is difficult to make out definitely in what way a chronic parenchymatous nephritis has begun. In other cases it is clearly the sequel of an acute affection. So far as microscopical investigation indicates it is possible that all the varieties of acute nephritis above described, except the suppurative form, may occasionally terminate in the chronic parenchymatous form. Moreover the various de-

generative processes described in Arts. 534–537 may be combined with secondary inflammatory changes, and so give rise to the morbid appearances of chronic nephritis.

VIRCHOW, FÖRSTER, LANGHANS, and FRIEDLÄNDER describe in certain cases of nephritis a multiplication of the nuclei of the glomerular capillaries, which may at times become very considerable. NAUWERCK has confirmed this by showing that the endothelial cells of the capillaries swell up and multiply (Fig. 209, Art. 540).

LITTEN (*Charité-Annalen* IV.) states that in the nephritis following scarlatina and relapsing fever concentrically stratified connective tissue is rapidly formed within Bowman's capsules. According to the account in the text this would appear to be, not new connective tissue, but stratified fibrin enclosing nuclei (Fig. 213 *g*).

545. The textural changes just described pass through various developmental stages, and thus in any given case one or another of them may be the most prominent. We may therefore distinguish certain anatomically distinct forms of chronic parenchymatous nephritis, depending on the stage of the process reached at the time the kidney is examined.

In the first form the connective tissue is but slightly altered (being simply infiltrated) while the epithelium of the tubules and in part of the glomeruli is highly fatty. This form is best described as the **inflamed fatty kidney,** or the kidney of fatty parenchymatous nephritis. The kidney is moderately swollen and soft, the cortex pale-gray and beset with numerous white opaque spots and streaks. The number and magnitude of these fatty patches depends on the degree of degeneration. They may be confined to the outer or to the inner zone of the cortex. The medulla is usually more or less reddened, often indeed cyanotic. If the cortical veins are full they show as red streaks, and the stellate veins show on the pale subcapsular surface as deep-red star-shaped blotches.

In a certain sense the **large mottled kidney** forms an antithesis to the fatty kidney. It is swollen, often considerably, and its surface is mottled with gray and red. On section the cortex looks broadened, moist, soft, and streaked with gray and grayish-red; the medulla is hyperæmic. Corresponding to its external appearance we find the tissue of the kidney in a condition of inflammatory œdema, the intertubular septa being in many places infiltrated with small cells. The glomerular epithelium is here and there swollen and desquamated, and in many of the tubules the epithelial cells are likewise cloudy, swollen, and desquamated. The fatty change is only moderately developed, the amount of fat present not sufficing to whiten the parenchyma.

When the kidney is much infiltrated and at the same time fatty, it is enlarged and the cortex is mottled with white patches; in extreme fatty change it may be all but uniformly white. This is the so-called **large white kidney.**

The differences between the three forms being rather differences of legree than of kind, there are naturally many intermediate varieties.

The external naked-eye appearance of the kidney depends greatly on he amount of blood it contains at the time of examination. Thus when he parenchyma looks red we must not at once conclude that there is io fatty degeneration, for when the latter is slight it may be quite disguised by the presence of hyperæmia. Conversely, mere paleness of he tissue is by no means a certain index of fatty change.

Hæmorrhage may accompany all forms of nephritis, but there is one articular form in which the hæmorrhage amounts to a characteristic; he cortex chiefly, the other parts in a less degree, being studded with ed and brown patches of extravasation. This form is therefore decribed as **chronic hæmorrhagic nephritis** (Fig. 213). The parenchyma may be altered in various ways; the most common change is a onsiderable degree of fatty degeneration with much infiltration of the ibrous stroma. The kidney is thus as a rule swollen and speckled with white, or almost uniformly white. There is usually much desquamation of the glomerular epithelium.

When the most marked character in a case of chronic nephritis is the morbid change in the glomerular epithelium, we might fitly describe it as **chronic glomerulo-nephritis.** When the accompanying degeneration of the tubular epithelium is slight the kidney may appear but very ittle altered, even though death has taken place from failure of the renal function; in such cases microscopic examination alone reveals the rue character of the disease. The changes in the glomeruli are the ame as those described in Arts. 544 and 540. In marked cases many of he glomeruli are obliterated.

543. **Terminations of chronic parenchymatous nephritis.** This disease not infrequently passes through the stages indicated in Arts. 544 and 545 and terminates in fatal suppression of the urinary function. In cases that are not speedily fatal the changes above described become more and more marked: which particular one of these changes is the most prominent depends on the individual peculiarities of the case.

The **fatty change** is not rarely the most extensive, the kidney becoming more and more of an unmixed white color as the grayish or reddish regions of fairly sound tissue diminish or disappear; the latter may at last be confined to the parts about the medullary rays. In such cases not only does the renal epithelium become fatty and perish, but oil-globules begin to appear in the walls of the glomerular and intertubular capillaries.

Often too the advancing fatty degeneration is accompanied by increased **cellular infiltration** of the connective tissue, so that the intertubular stroma becomes transformed into a series of swollen cellular columns.

At an early stage **atrophy of the secreting structures** begins in

the regions most affected. The tubular epithelium may in consequence of the degenerative changes be lost altogether, the denuded tubules becoming therefore collapsed and functionless. This is however by no means invariably the case, for it frequently happens that in the absence of other complications the fatty and desquamated cells are replaced by the regenerative multiplication of the remaining ones. Destruction of the glomeruli is a more serious danger, for it involves not only the suppression of the urinary secretion but also the partial interruption of the intertubular circulation. The glomeruli may be rendered functionless by an excessive accumulation of loose epithelium and exuded liquid within their capsules, leading to compression of the capillaries. More commonly however the injury is primary, and due to hyaline swelling of the capillary-walls and in part to thrombosis of their channels. The epithelium always perishes, partly by desquamation, partly by fatty degeneration and disintegration. Sometimes a certain amount of fibrous hyperplasia occurs in the neighborhood of the obliterated glomeruli, and the capsules thus appear abnormally thickened.

These localized atrophic changes in the secreting structures are sooner or later followed by **cicatricial contractions** of the external surface. They are seldom quite absent in the large white kidney, and in some cases are so numerous as to give the organ a granulated appearance while its volume becomes less than normal. This is of course possible only in cases of long standing, in which the changes in the parenchyma have spread so gradually that its functions have at no time been interrupted. Such cases both in their clinical course and histological characters approach those which we class under the head of renal cirrhosis or indurative nephritis with contraction.

Chronic Indurative Nephritis.

547. **Chronic indurative nephritis** or **renal cirrhosis** is distinguished anatomically by the fact—that the inflammatory process issues in hyperplasia of the renal connective tissue, and consequent induration or cirrhosis of the parenchyma.

In chronic parenchymatous nephritis there is a certain amount of fibrous overgrowth, but this is of altogether minor importance in comparison with the other results of the inflammatory process. In indurative nephritis on the other hand it is this fibrous overgrowth and the resulting cirrhosis which is the essential characteristic of the affection.

The disease sometimes commences acutely, but its onset is usually very gradual and insidious. In either case the appearance in the stroma of small patches of cellular infiltration is the most important of the initial changes. This infiltration is moreover always accompanied by degeneration of the epithelium, though the extent and intensity of this varies much in different cases, a fact which in the main explains the

diverse clinical phenomena exhibited in connection with the onset of the disease.

In like manner there are differences in the amount of inflammatory œdema accompanying the infiltration, and corresponding differences in the extent to which the kidney is swollen.

When the interstitial hyperplasia has continued for some weeks or months cicatricial patches appear, and as they contract give rise to depressions and puckerings of the outer surface of the kidney. These contractions are more or less numerous and extensive according to the extent of the original infiltration. The kidney is either anæmic and pale-gray in tint, or hyperæmic when it appears grayish or brownish red; its size may be normal or increased or diminished; at a later stage it is harder, tougher, and denser than in health.

The cortex is always thinned at the site of the cicatrices; elsewhere its thickness may be normal or even increased, but it is never very much increased. The cortex on section has the same tint as the surface. The pale white patches of fatty degeneration may be entirely absent, though not infrequently they may be detected in varying number within the cortical zone. The medullary zone is usually redder than is normal.

The connective tissue is hardened and overgrown not merely within the cicatrices but also at various points in the deeper layers of the cortex: the secreting structures are atrophied (Fig. 214).

The indurated patches lie chiefly in the neighborhood of the small veins, though they may be distributed irregularly throughout the region of the labyrinth.

The first stage of the indurative change is the appearance of the disseminated cellular infiltration (*l*) of the stroma. Then the intertubular tissue (*k*) becomes more or less notably increased and fibrous: it often becomes thickly beset with small round-cells, or at least the nuclei are much more numerous than usual.

The capsules of the glomeruli in the affected region are in general considerably thickened, and appear to be made up of nucleated fibrous tissue arranged in concentric layers (*a*). It is however to be noted that the amount of thickening varies greatly: in some cases it is enormous, in others very slight. The latter is observed in instances where the infiltration is mainly around the small veins, the former where it is more uniformly diffused over the whole of the labyrinth.

The tunica adventitia of the blood-vessels (*n o*) is usually more or less thickened. Sometimes the thickening extends to the inner coats also, and leads to obstruction of the vessel. A certain number of the capillaries always become impermeable as the change progresses.

The glomerular epithelium in recent cases is seen to be swollen or loosened and desquamated (*f*), though this change is seldom so marked as in the forms of nephritis already described: it is also rare for the capsular epithelial cells to show signs of any great degree of multiplication

or of desquamation. When there is much thickening of the capsule, or much disturbance of the circulation through obstruction of the capillaries or narrowing of the vasa afferentia, the glomeruli begin to atrophy. The capillary loops lose their epithelium (*c*), and are transformed into pale hyaline or finely-granular denucleated (*d*) structures, which are impermeable by the blood or by artificial injections.

During the progress of the disease the glomeruli excrete albuminous urine, which usually flows off into the tubules; sometimes however it coagulates in the presence of the shed epithelial cells and gives rise to the stratified fibrinous and nucleated masses (*e*), which we have already described as surrounding the glomerular vessels. The albuminous urine often contains extravasated red and white blood-cells.

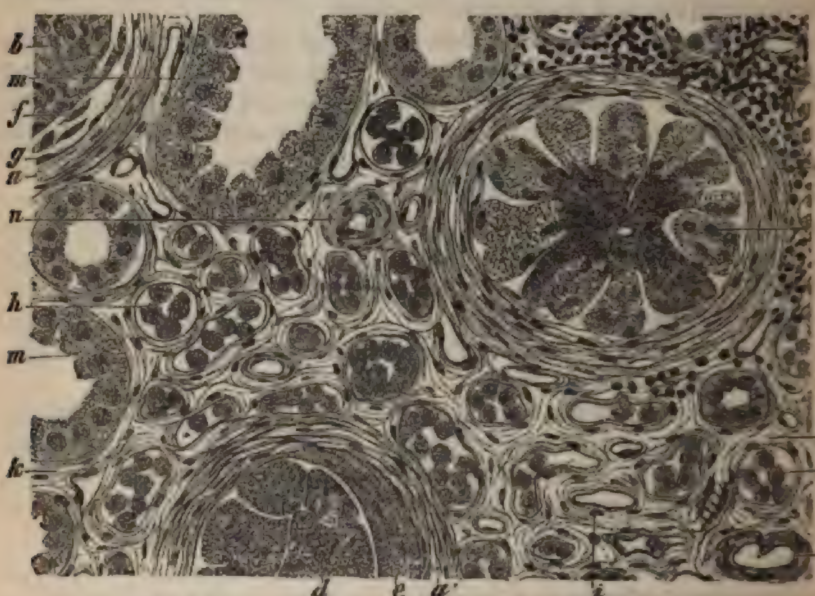


FIG. 214. INFLAMMATORY INDURATION AND ATROPHY OF THE RENAL TISSUE.

(*Section treated with alcohol and alum-carmine, and mounted in Canada balsam:* × 250.)

a, capsule of Bowman thickened and fibrous
b, normal glomerulus
c, glomerulus with vessels partly obstructed and hyaline, the epithelium being nearly all destroyed
d, obliterated glomerulus
e, nucleated coagulum composed of fibrinous exudation and shed epithelium
f, glomerular epithelium loosened and shed
g, capsular epithelium
h, collapsed tubule with atrophied epithelium
i, collapsed and denuded tubule
k, hyperplastic fibrous stroma
l, cellular infiltration
m, normal tubule somewhat dilated
n, vas afferens.
o, small vein

The tubular epithelium undergoes the same forms of degeneration as we have described in connection with parenchymatous nephritis, though the degeneration is usually less intense and less wide-spread: in cases of no very long standing we therefore find the greater number of the tubules still healthy.

By the time that new fibrous tissue has been formed at a particular spot, the corresponding tubules are usually advanced in atrophy. The lumen is narrowed, the secreting epithelium represented by small cubical cells lining the walls or lying loose within the lumen (*h*). Many tubules are empty and collapsed, their epithelium having altogether disappeared (*i*).

The degeneration and atrophy of the tubules is due partly to the disturbances of circulation and nutrition caused by the inflammatory changes, partly to the destruction of the glomeruli (Art. 524).

The contents of the unaffected tubules are the same as in parenchymatous nephritis, though fewer of them contain casts and masses of epithelial detritus. Hæmorrhages and pigmentary deposits are likewise less common.

Indurative nephritis and the cirrhotic contracted kidney (Art. 548) correspond partly to the form described by clinical observers as true contracted kidney, partly to so-called secondary contracted kidney. The term "true contracted kidney" has been made to include the arteriosclerotic contracted kidney (Art. 526), whose mode of origin is totally different from that of the cirrhotic contracted kidney. Confusion thus arises, and it may therefore be well in future to avoid the use of the clinical term.

The term "secondary contracted kidney" is applied to cases which begin acutely. This distinction is valueless from the point of view of the morbid anatomist, as such cases differ in no essential respect from those whose onset is gradual or undiscerned.

548. **Terminations of chronic indurative nephritis.** When this affection is not speedily fatal from the extension of the accompanying epithelial degeneration, it may lead in the course of months or years to very extreme induration and obliteration of the secreting structures. The kidney is then always diminished in size, often remarkably so; the capsule is adherent; the surface granulated. The 'granulations' may be coarse or fine, regular or irregular (Fig. 215 *A*).

The tint of the protuberant **granulations** varies greatly, depending on the amount of blood present in the cortex and on the degree of fatty change in the epithelium. It is usually grayish-red, sometimes however it is gray or mottled gray and white, or almost entirely white and opaque. The depressions and contractions are usually somewhat redder.

The renal tissue is dense and tough, the cortex thinned, the papillæ often truncated or stunted. The tint of the cut surface corresponds with that of the external surface: the medulla is generally somewhat redder, but not infrequently it has much the same tint as the cortex.

The cortical zone is always traversed by fibrous bands with small islands of less altered or persistent normal tissue lying between them (Fig. 215 *A*).

The fibrous bands start from the intergranular depressions of the surface (*B*) and run towards the bases of the medullary papillæ, be-

ing interconnected by numerous transverse bands; the islands of normal tissue are therefore more frequently rounded or oval than elongated. The fibrous bands run in general along the course of the veins, though they frequently ramify without any apparent regularity through the labyrinth. The more numerous they are the smaller of course are the islands enclosed in their meshwork. Cases are met with in which the greater part of the labyrinth is thus indurated and obliterated, the only parts retaining their function being parts of the medullary rays and the tissue immediately adjoining. In such cases the surface granulations

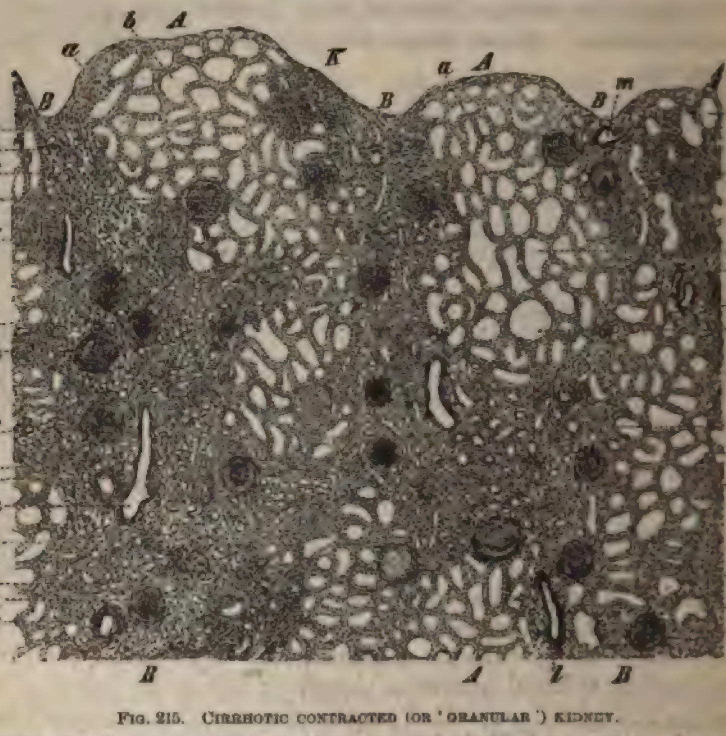


FIG. 215. CIRRHOTIC CONTRACTED (OR 'GRANULAR') KIDNEY.

(Vertical section through the outer zone of the cortex, stained with alum-carmine and mounted in Canada balsam × 40.)

A, persistent renal tissue giving rise to 'granulations.'
B, cicatricial bands giving rise to depressions and contractions.

a, normal tubules
b, dilated tubules
c, cysts
d, normal glomeruli
e, atrophied and collapsed tubules filled with loose epithelium
f, atrophied empty tubules
g, hyperplastic fibrous tissue
h, atrophied glomeruli with thickened capsule
i, the like with normal capsules
k, cellular infiltration
l, arteriole
m, venule

are naturally very fine and regular; where the cirrhosis is confined to the course of the veins the irregularities of the surface are usually much

more marked. The course and mode of extension of the indurative change are in fact very similar to what is observed in cirrhosis of the liver (Art. 496).

The fibrous bands of the cortex always enclose atrophied and collapsed tubules (*e f*) and obliterated glomeruli whose capsules are more or less thickened (*h i*). These bands are thus simply portions of renal tissue of which the secreting structures are rendered functionless and the stroma hyperplastic by chronic inflammation. Here and there a tubule or a glomerulus may persist within the indurated region, while some of the tubules are dilated into cysts by the retention of already secreted urine (*c*).

The islands of persistent secreting tissue may present a normal appearance (*a*). More frequently some of the tubules and glomeruli show signs of compensatory hypertrophy (*b*). Some of the epithelial cells are fatty, though the extent of this change varies much in different cases. Here and there too we find patches of cellular infiltration (*k*), a sign that the inflammatory process is kept up.

Both in the cortex and in the medulla are seen tubules containing hyaline cylinders, or masses of shed epithelium and extravasated leucocytes.

The induration of the intertubular stroma and the loss of the glomeruli involve the obliteration of a considerable portion of the vascular system of the cortex. The vessels passing into the medullary zone (Art. 526) consequently become dilated, though the channels thus opened up never fully compensate for the loss of the cortical channels.

Tuberculous and Syphilitic Nephritis.

549. **Tuberculosis of the kidney** is in most cases due to embolic infection. In rare instances primary tuberculosis of the bladder, prostate, spermatic duct, or testicle may extend to the kidney by way of the ureter.

Acute miliary tuberculosis and chronic localized tuberculosis are the two forms of the affection.

Miliary tuberculosis of the kidney is merely a part of a general eruption of tubercle in the various organs of the body. Wherever the tuberculous virus lodges, in cortex or medulla, there appears a small semi-translucent grayish speck, which presently grows into a gray nodule. This then becomes whitish, and is often surrounded by a hæmorrhagic areola. The whitish tinge is due partly to infiltrated leucocytes, partly to turbid swelling and necrosis of the epithelium set up by the action of the bacilli. When the cellular infiltration becomes great the renal tissue-elements within the infiltrated area perish.

The number of tubercles appearing in the kidney is sometimes very

great, sometimes small. Occasionally the tubercles are confined to the region supplied by a single twig of the renal artery.

Chronic localized tuberculosis of the kidney begins, like the miliary form, at the spot whither the bacilli have been carried by the blood-stream. This may be either within the parenchyma or in the mucous membrane of the calices or pelvis.

At this spot gray nodules are formed, and presently become caseous. In the course of weeks or months they grow into large irregular nodes by progressive marginal infiltration, while new nodules develop in the tissue around. In the mucous membrane of the pelvis the process extends partly as a diffuse infiltration, partly as a nodular eruption. The nodules and the infiltrated tissue ultimately become necrosed and caseous, and presently disintegrate.

After a time the kidney appears studded with gray nodules and white opaque nodes, the larger of these being softened and excavated. The medullary papillæ are many of them caseous and broken down, the pelvis appears enlarged by the excavations, and in places is continuous with the tuberculous cavities of the parenchyma. The mucous membrane is infiltrated, thickened, and gray, its surface here and there necrotic and covered with yellow sloughing ulcers; or the deeper layers being uniformly infiltrated and thickened, the entire mucous membrane may be transformed into a cheesy broken-down ulcerous mass.

The tuberculous process frequently extends to the ureter, transforming it into a more or less gristly tube with thickened walls. The inner surface is either white necrotic and ulcerated throughout its entire extent, or it is gray and infiltrated, and studded with scattered patches of necrosis and ulceration.

In the more advanced stages of the disease the kidney appears somewhat enlarged, the capsule adherent, and the surface often rough and irregularly nodulated. Cheesy and granular detritus occupies the pelvis, which latter by excavation or by retention of urine is abnormally large. In extreme cases the entire kidney is destroyed, nothing remaining but a thick-walled sack containing cheesy or puriform detritus.

As a rule both kidneys are affected, though it is common to find the process much more advanced in one kidney than in the other.

550. **Syphilitic affections of the kidney** exhibiting any special or characteristic features are not common. Renal inflammation referable to the influence of the syphilitic poison is however occasionally met with, and is characterized by the formation of coarse cicatricial bands and of caseating gummata.

In congenital syphilis induration and contraction of the kidney has in somewhat rare instances been observed.

References on renal tuberculosis:—RAYER, *Maladies des reins* Paris 1840; VIRCHOW, *Krankhafte Geschwülste* II.; SCHMIDTLEIN, *Deutsche Klinik* 1863; KUSSMAUL, *Würzburger med. Zeitschr.* IV.; ROSENSTEIN, *Berl. klin. Woch.* 1865;

COLIN, *Gazette hebdom.* x.; SOUTHEY, *Brit. Med. Journ.* 1, 1867; MOSLER, *Arch. d. Heilk.* 1863; E. HOFFMANN, *Deutsch. Arch. f. klin. Med.* III.; HUBER, *ibid.* IV.; KLEBS, *Handb. d. path. Anat.*; EBSTEIN, *Ziemssen's Cyclop.* XV.; ARNOLD, *Virch. Arch.* vol. 83; GAULTIER, *La tuberculose rénale primitive* Thèse de Paris 1882; DICKINSON, *Renal and urinary affections* III. London 1885; STEINTHAL, *Virch. Arch.* vol. 100; HILTON FAGGE, *Principles and practice of medicine* II. London 1886.

On renal syphilis see VIRCHOW, *Krankhafte Geschwülste* II.; CORNIL, *Journ. de l'anat.* 1865; MOXON, *Guy's Hosp. Rep.* 1868; LANCEREAUX, *Treatise on syphilis* I. (New Syd. Soc.) London 1868; GREENFIELD, *Atlas of Path.* (New Syd. Soc.) London 1879; NEGELL, Thèse de Paris 1884; KLEBS, *loc. cit.*; CORNIL and RANVIER, *Man. d'hist. path.* Paris, 1878, *Man. Path. Hist.* II. London 1886; the latter found in one case a number of gummata, some of them as large as a pea.

In syphilitic patients we not infrequently find the kidney in a state of amyloid degeneration (MOXON, *loc. cit.*).

In tuberculosis of the urinary organs ROSENSTEIN and BABES (*Cent. f. d. med. Wiss.* 1883) have demonstrated the presence of tubercle-bacilli in the urine.

CHAPTER LXX.

RENAL CYSTS AND HYDRONEPHROSIS.

551. **Renal cysts.** When a urinary tubule is obstructed by a uratic deposit, a tube-cast, a cicatricial band, or other cause, the urine may accumulate behind the obstruction and distend its lumen into a cyst. The like may happen to a glomerular capsule when the mouth of its tubule is blocked.

Kidneys otherwise normal occasionally contain smooth-walled cysts varying in size from that of a pea to that of a walnut and protruding more or less above the surface of the organ. Cysts are however much more frequently met with in diseased kidneys, and especially in the contracted forms due to cirrhosis and arteriosclerosis. THORN states that cysts may also be due to inflammation of the pelvis or calices of the kidney extending by continuity to the stroma of the medullary papillæ. In fact it would appear that the compression and obstruction of the tubules resulting from inflammatory change in the tissue about them lead much more frequently to the formation of cysts than internal blocking of the lumen by concretions or deposits. Where a certain amount of constriction has already taken place such internal obstruction may no doubt make the occlusion complete.

The number of these cysts found in a single kidney varies greatly. Cases occur in which they are so numerous as to occupy the whole organ, mere shreds or septa of renal tissue separating the contiguous cavities (cystic degeneration).

The largest cysts met with in kidneys altered by nephritis are about the size of a cherry, the smallest are microscopic. It frequently happens that none are larger than a pea, though in exceptional instances two or more coalesce to form a single cavity.

The larger cysts have thin translucent walls, the inner surface being smooth, and the contents clear or yellowish-brown or slightly blood-stained liquid generally containing urinary salts. The smaller cysts met with in contracted kidneys not infrequently contain a colloid substance. All cysts are lined with epithelium, the cells being usually flattened, rarely columnar.

When the cysts are both large and numerous the kidney may have the look of a large tumor. This condition is sometimes developed before birth, the child being born with kidneys transformed into relatively

enormous honeycombed tumors representing an extreme degree of cystic degeneration: this is referred to as **fœtal cystic disease.** The tumors may be so large as to interfere with delivery. According to VIRCHOW the condition is sometimes due to inflammatory occlusion and atrophy of the papillæ; but THORN thinks it is more frequently brought about by inflammation extending to the substance of the papillæ from the calices. Absence of the pelvis or occlusion of the ureters may also have the like effect. Some authorities hold that the condition is due to a primary fault of development.

References:—BRIGHT, *Memoirs on abdominal tumors* (New Syd. Soc.) London 1860; ROKITANSKY, *Lehrb. d. path. Anat.* III. 1861; BECKMANN, *Virch. Arch.* vol. 9; FRERICHS, *Die Bright'sche Nierenkrankheit* Brunswick 1851; SIEBOLD, *Monatsschr. f. Geburtskunde* 1854; VIRCHOW, *Gesam. Abhandl.* Frankfort 1856, *Virch. Arch.* vol. 46; BRÜCKNER, *ibid.*: HERTZ, *ibid.* vol. 30; SIMON, *Med. chir. Trans.* XXX.; KOSTER, *Dublin Quart. Journ.* XLVI.; EVE, *Trans. Path. Soc.* XXXI. (1860); THORN, *Beitrag z. Genese d. Cystenniere* In. Diss. Bonn 1882; CHOTINSKY, *Ueber Cystennieren* In. Diss. Bonn 1882 (this author affirms that in fœtal cystic kidney the occlusion of the tubules is to a great extent due to excessive multiplication of the epithelial cells); CORNIL and BRAULT, *Path. du rein* Paris 1884; DICKINSON, *Renal and urinary affections* III. London 1885 (with cases); CORNIL and RANVIER *Man. Path. Hist.* II. London 1886. A number of cases are described in the *Transactions of the Pathological Society.*

552. **Hydronephrosis.** When the escape of the urine from the pelvis of the kidney is prevented or obstructed, it accumulates and distends that cavity, giving rise to what is called hydronephrosis or dropsy of the kidney.

Renal calculi impacted in the ureter, stricture or twisting of the ureter, valvular folds of mucous membrane, or compression by the gravid uterus or by uterine ovarian and vesical tumors, enlarged prostate, urethral stricture, and phimosis—are all possible causes of the condition. In new-born infants the cause of the obstruction is usually some anomaly of the ureter, malposition of the kidney, valvular folds in the ureter, constriction or occlusion of the urethra, enlargement of the prostate or colliculus seminalis, or phimosis.

The pelvis and calices are sometimes enormously distended, forming a sack large enough to fill the greater part of the abdomen and containing 10 to 20 litres of liquid. The part of the ureter above the obstruction is dilated in like manner.

The first result of this accumulation of liquid is the flattening of the papillæ and thinning of the cortex of the kidney. The parenchyma persists for a considerable time but at length undergoes atrophy, the tubules being reduced to flattened or cleft-like channels lined with compressed epithelium, and ultimately with the glomeruli becoming functionless and obliterated. In extreme cases the renal tissue is reduced to a thin film or in part disappears altogether, the sack consisting in great

measure merely of fibrous tissue, which in cases of old standing may be of remarkable thickness.

At first the liquid is simply urine; but as the pressure increases less and less urine is excreted, and when the renal tissue atrophies the excretion ceases altogether. The sack however continues to increase in size, owing to the secretion of liquid by the mucous membrane of the pelvis and calices. This liquid contains no urinary matters, but is albuminous; and sometimes it is tinged with blood. Colloid masses and cholesterin are also found in some cases.

Hydronephrosis is usually confined to one side, it is rarely bilateral. When the obstruction affects only a part of the pelvis of the kidney, or when there are two pelves, the hydronephrosis may be partial.

References:—VIRCHOW, *Gesamm. Abhandl.* Frankfort 1856; SÄXINGER, *Prager Vierteljahrsschr.* 1867; ACKERMANN, *Deut. Arch. f. klin. Med.* I.; HELLER, *ibid.* V.; HILDEBRAND, *Sammlung klin. Vorträge* 5; GUSSEROW, *ibid.* 18; SIMON, *ibid.* 88; STADFELDT, *Monatsschr. f. Geburtskunde* 1862; FARRE, *Lancet* 2, 1861; MORRIS, *Med. chir. Trans.* LIX. (1876); EBSTEIN, *Ziemssen's Cyclop.* XV.; AUFRECHT, *Die diffuse Nephritis* Berlin 1879 (this author tied the ureter in animals, and observed degeneration of the renal epithelium and afterwards multiplication of the connective-tissue cells); DICKINSON, *loc. cit.*; ROBERTS, *Urinary and renal diseases* London 1885 (with references and cases).

CHAPTER LXXI.

PYELITIS AND PYELONEPHRITIS.

553. When irritant substances are excreted by way of the kidney they frequently set up inflammation in the mucous membrane of the pelvis (**pyelitis**) and ureter. Thus catarrhal, croupous, and diphtheritic inflammation of this membrane may follow or accompany typhoid, scarlatina, small-pox, pyæmia, diphtheria, cholera, nephritis, etc. and the use of drugs like cantharides, copaiba, cubebs, turpentine, etc. When the irritant matter ceases to be excreted the inflammation usually comes to an end also.

These secondary or symptomatic inflammations are not so serious as the more independent and progressive inflammations set up and maintained by the presence in the renal pelvis of parasitic organisms or urinary concretions.

In speaking of parasitic pyelitis we note in passing that tuberculous pyelitis, already described (Art. 549), is due to the invasion of a bacillus. In like manner micro-organisms give rise to the pyelitis which sometimes accompanies suppurative or septic nephritis. Another purulent or suppurative variety is caused by the action of micro-organisms reaching the pelvis from the bladder through the ureter. The latter micro-organisms are usually micrococci, though bacilli and filamentous fungi may also reach the kidney by this channel. They enter the bladder as a rule through the urethra, but cases occur in which they break into it from abscesses in the rectum, uterus, vagina, or pelvic connective tissue.

Bacteria are often introduced into the bladder by means of dirty catheters. In other instances they attack the urethra primarily (as in gonorrhœa), and extend gradually as far as the bladder.

Their lodgment in the bladder is favored if there be any interference with the evacuation of the urine, such as is caused by stricture or paralysis. When the bladder is incompletely emptied so that some urine remains in it for a considerable time the bacteria which enter it find time to multiply and set up changes in the urine. As the urine accumulates and the ureters become dilated the bacteria find ready access to the pelvis of the kidney through these channels.

Animal parasites, as well as vegetable, may induce inflammation in the pelvis and ureter. This is especially true of *Bilharzia* or *Distoma*

hæmatobium (Art. 239), whose eggs are deposited and embryos hatched in the urinary tract. *Eustrongylus gigas* (Art. 231) is much less dangerous.

All the forms of concretion described in Arts. 531 and 532 are capable of exciting more or less intense pyelitis. They give rise to continuous mechanical irritation, which in the case of the hard and spiny oxalate-calculi is often very great, and is not slight in the case of the other forms. They produce mischief in another way when they become impacted in the ureter and cause retention of urine as well as local lesions.

554. Pyelitis, set up in the various ways just described, varies much in its symptoms and course. In catarrhal inflammation the mucous membrane is red and swollen, often studded with small extravasations, and secreting a liquid abounding in epithelial cells or pus according to the stage of the disorder. The lymphadenoid tissue existing in variable quantity in the submucosa is often swollen, and appears in the form of gray nodular swellings in the reddened mucous membrane. In chronic cases ulceration and thickening takes place. When the inflammation is diphtheritic patches of the mucous membrane rapidly slough. Bacteria have a very destructive action, as the urine becomes alkaline owing to their multiplication in it, and the products of the decomposition corrode the inflamed tissue. Sooner or later the bacteria invade the renal parenchyma. According to KLEBS they advance along the collecting tubes and tubules destroying the epithelium and exciting inflammation.

As a result of this invasion the kidney swells up, often enormously, and looks as if soaked or sodden. At the same time in the cortex and medulla appear a number of small yellow patches surrounded by a zone of hyperæmia, which are simply small patches of suppuration. Purulent pyelitis thus gives rise to **purulent pyelonephritis** (or so-called 'surgical kidney'). The process may issue in induration, but more commonly the suppurating patches grow into large abscesses which burst into the pelvis of the kidney. Not infrequently abscesses form in the tissue immediately surrounding the kidney, and are called **perinephritic abscesses.** If the suppuration within the kidney goes on large pus-secreting cavities communicating with the renal pelvis are produced, and in extreme instances the whole of the kidney is thus destroyed, its place being occupied by a mere pus-containing sack. This condition is referred to as **pyonephrosis.**

Parasitic pyelonephritis may be unilateral or bilateral; in the latter case it is usually more advanced on one side than on the other.

555. **Calculous pyelitis** leads partly to thickening and induration of the affected tissues, partly to ulceration. Not infrequently the inflammation, at least during some part of its course, becomes purulent: occasional hæmorrhages are also common.

The inflammation sooner or later extends to the renal parenchyma

and leads to swelling and cellular infiltration, terminating in suppuration or in fibroid induration. In either case some portion of the renal tissue is destroyed. The whole of it may perish in extreme cases, leaving nothing but a fibrous sack surrounding the original calculus. Perinephritic abscesses also are frequently produced.

When calculi of some size become wedged in the ureter the outflow of urine may be interrupted. If in consequence of this a considerable accumulation of urine takes place in the pelvis of the kidney we may have hydronephrosis (Art. 552) superimposed on pyelitis. The retained urine often decomposes and thus intensifies the inflammation so that it becomes purulent: in this way pyonephrosis succeeds hydronephrosis.

The impacted stone may be gradually urged forward into the bladder by the pressure of the accumulating urine, giving rise to hæmorrhage, erosion, and inflammation on its way.

The ulcers, whether of the ureter or pelvis, may break through externally and thus enable pus to escape into neighboring parts, such as for instance the intestine or the bladder. More often however the pus escapes into the perinephric (subperitoneal) cellular tissue, and gives rise to wide-spread suppurative or septic inflammation.

Calculous pyelitis is usually unilateral, rarely bilateral.

References:—MICHAELIS, *Wien. med. Presse* XI.; EBSTEIN, *Ziemssen's Cyclop.* XV.; BRIGHT, *Abdominal tumors* (New Syd. Soc.) London 1860; Discussion, *Internat. med. congress* London 1881 and *Lancet* 1, 1882; J. B. ROBERTS, *Amer. Journ. med. sciences* April 1883 (on perinephritic abscess); ROBERTS, *Urinary and renal diseases* London 1885.

CHAPTER LXXII.

RENAL TUMORS AND PARASITES.

556. Of the various primary **connective-tissue tumors** of the kidney **sarcoma** presents the greatest interest. Renal sarcoma is usually congenital, and is apparent at birth or becomes noticeable in the first months or years of life. The tumor is sometimes very large (4 to 6 kilogrammes), and consists of soft whitish tissue interspersed with patches of hæmorrhagic softening. The mass of the tissue is made up of round, spindle-shaped, and multiform cells. It sometimes contains large transversely-striated spindles (rhabdomyoma, Art. 153). These last have a special interest, for they are evidence that the tumor has arisen in tissue the early stages of whose development have in some way been disturbed (Art. 516).

Cellular **fibromata** are frequently met with in the kidney, and take the form of nodules of the size of a pea or smaller. Large fibrous tumors are very rare, as are also myxomata, lipomata, angiomata, and their combinations. They all of them take the form of nodes seated in the parenchyma or on the capsule of the kidney, or in its pelvis or calices. GRAWITZ has investigated certain small subcapsular tumors, from the size of a pea to that of a cherry, and of a white marrow-like appearance, which have been described as lipomatous: he regards them as simply aberrant and proliferous portions of the suprarenal body. In their structure they are very like the degenerate suprarenals described in Art. 565, consisting of a fibrous stroma with rows and groups of cells containing a variable amount of fat. GRAWITZ has named them "*strumæ lipomatodes aberratæ renis.*" Telangiectatic tumors (angiomata) in the renal pelvis sometimes give rise to severe hæmorrhage.

Adenomata of the kidney appear as well-defined white nodes of the size of a walnut or less, and with a structure like that of ovarian adenomata. WEICHSELBAUM and GREENISH distinguish a papillary and an alveolar variety. The former they say starts in the collecting tubes, and consists of gland-like tubules and acini, studded internally with papillæ and lined with cylindrical epithelium. The alveolar form is said to start in the convoluted tubules and is lined with epithelium like theirs. It is very probable that these growths may develop into carcinomata.

Cancers of the kidney are either soft or hard, and lead to greater or less enlargement of the organ; sometimes the enlargement is very great. In the larger tumors the whole of the renal epithelium may be destroyed by the cancerous growth. The latter may extend into the pelvis. The

smaller tumors affect only a portion of the parenchyma and are often fairly well marked off from the sound tissue. The tumors commonly enclose softened and hæmorrhagic patches, whence blood and cancerous detritus may reach the urine. Renal carcinoma occurs at all ages, but is relatively frequent in children. In general it is unilateral, though cases are recorded in which a smaller tumor has been found in the second kidney.

Sarcoma and carcinoma are not infrequent as secondary or metastatic growths: they form rounded nodes.

References on myosarcoma:—EBERTH, *Virch. Arch.* vol. 55; COHNHEIM, *ibid.* vol. 65; BRODOWSKI, *ibid.* vol. 67; MARCHAND, *ibid.* vol. 73; BROSIN, *ibid.* vol. 96; KOCHER and LANGHANS, *Deut. Zeitschr. f. Chir.* IX.; LANDSBERGER, *Berl. klin. Woch.* 1877; OSLER, *Journ. of Anat. and Physiol.* XIV.; HUBER and BOSTRÖM, *Deut. Arch. f. klin. Med.* XXIII.; EVE and WILLIAMS, *Trans. Path. Soc.* XXXI. (1882): on primary sarcoma—WINDLE, *Journ. of Anat. and Physiol.* XVIII. (with index of cases); SMITH, *Amer. Journ. med. sci.* 1886.

On lipoma and 'struma':—VIRCHOW, *Krankh. Geschwülste* II.; KLEBS, *Handb. d. path. Anat.*; STURM, *Arch. d. Heilk.* 1875; SABOURIN, *Arch. de physiol.* IX.; GRAWITZ, *Virch. Arch.* vol. 93; EBSTEIN, *Ziemssen's Cyclop.* XV.; RICKARDS, *Brit. Med. Journ.* 2, 1883.

On adenoma and carcinoma:—ROBIN, *L'epithelioma du rein* Paris 1855; WALDEYER, *Virch. Arch.* vols. 51, 54; KLEBS, *loc. cit.*; PEREWERSEFF, *Virch. Arch.* vol. 59; WEIGERT, *ibid.* vol. 67; KÜHN, *Deut. Arch. f. klin. Med.* XVI.; STURM, *Arch. d. Heilk.* XVI.; NEUMANN, *Essai sur le cancer du rein* Paris 1873; ROHRER, *Das primäre Carcinom d. Niere* In. Diss. Zurich 1877, *Virch. Arch.* vol. 67; WEICHSELBAUM and GREENISH, *Wien. med. Jahrb.* 1883; MOORE, *Trans. Path. Soc.* XXXI. (1882); Report, *Brit. med. Journ.* 1, 1884.

557. Of the **animal parasites** inhabiting the kidney *Echinococcus* is the most important. It forms hydatid cysts from the size of a hazelnut to that of a child's head, with or without daughter-cysts. The cysts may burst into the pelvis of the kidney. When the scolices die the cyst may contract, and its contents become inspissated and cretaceous.

Cysticercus cellulosæ and *Pentastoma denticulatum* are very rare. When the blood contains *Filaria* a number of the parasites reach the kidney, lying both without and within the vessels. Their presence in the kidney and in the thoracic duct gives rise to intermittent hæmaturia and chyluria, the urine in the latter case being milky from the admixture of excessively fine oil-globules (Art. 235).

Eustrongylus gigas and *Bilharzia* or *Distoma hæmatobium* have already been alluded to (Art. 553). The eggs of the latter when deposited in the mucous membrane of the pelvis or ureter excite inflammation resulting in ulceration and induration. The more superficial may become encrusted with urinary salts and form sandy grains on the mucous membrane.

When ulceration of the intestine and of the ureter or renal pelvis leads to the formation of abnormal communications between these parts, round-worms occasionally wander into the kidney.

CHAPTER LXXIII.

DISORDERS OF THE BLADDER.

558. **The urinary bladder** is the temporary receptacle of the renal secretion. When the urine is mingled with abnormal exudations from the blood-vessels, or the products of morbid change in the kidney or its pelvis, these are naturally detained for a certain time in the bladder. Of the formed matters thus occurring in its contents the following are the most important.

Red blood-cells or their detritus come either from the kidney or from its pelvis. In the former case they have in general escaped from the glomeruli as a result of disordered circulation (Arts. 523, 527) or of inflammation (Art. 544). They are rarely derived from intertubular hæmorrhage. Vascular tumor-growths in the kidney (such as carcinoma or angioma) may also give rise to hæmorrhage and hæmaturia.

When a part of the extravated blood coagulates in the tubules the urine contains dark and opaque granular cylinders containing blood-cells or their remains and known as **blood-casts.**

Hæmorrhage from the pelvis of the kidney is generally due to inflammation and erosion caused by renal concretions.

White blood-cells appear in the urine in inflammatory conditions of the kidney and its pelvis, especially in purulent pyelitis. In chronic suppuration they are for the most part fatty and disintegrated. In tuberculous and other necrotic affections we find bacilli and necrotic detritus in the urine.

Epithelial cells come from the pelvis and from the collecting tubes of the kidney, perhaps too from the loops of Henle and the intercalary tubules. The statement sometimes made—that entire and unaltered epithelial cells from the convoluted tubules escape into the urine—is erroneous. Degenerate cells from the cortex and their detritus are however met with.

The pelvic epithelial cells are polymorphous, resembling exactly those of the bladder itself. The renal cells are cylindrical or cubical: when they are in great numbers and cohere into cylinders we have the so-called **epithelial casts.**

In rare cases **cancer-cells** from a renal tumor are found in the urine.

When albuminous matters escape into the tubules with the urine and there coagulate, we have formed, as already described (Art. 533), the cylindrical masses known as **tube-casts;** and some of these are usually washed out and reach the bladder. They are either entirely colorless and hyaline, or granular, or waxy in appearance and tint. Casts of each of these forms may have adhering to them epithelial cells or their detritus (albuminous and fatty granules), free nuclei, white and red blood-cells, granular deposits of urinary salts, and crystals of calcium urate or oxalate.

When there are **bacteria** in the urine some of them may adhere to the casts: it is however to be noted that the granular masses enveloping some of the casts have of late been erroneously taken for micrococci.

All the urinary deposits and concretions described in Arts. 531 and 532 are ultimately carried into the bladder, unless their size prevents them passing through the ureter. **Scolices** and daughter-cysts occasionally escape from a renal hydatid. And when the ova of *Bilharzia* or *Filaria* are deposited in the mucous membrane of the urinary tract we are apt to find both **ova** and **embryos** in the urine.

559. When the urine has reached the bladder it is liable to be mingled with abnormal products derived either from the diseased bladder-wall or the parts adjoining, or from the exterior.

Blood is one of the most common admixtures, and is met with in cases of intense inflammation, ulceration, or engorgement of the wall of the bladder, and in the vascular lesions accompanying scurvy, hæmorrhagic small-pox, scarlatina, etc. Not infrequently traumatic lesions such as are caused by stone or external violence, and tumors such as papilloma, sarcoma, and cancer, are the cause of vesical hæmorrhage.

Vesical epithelium is shed into the urine in inflammation (cystitis) and in cases of papillomatous (so-called villous) tumor. In the latter instance villous fragments of the growth are also occasionally found. Masses of **cancer-cells** are frequently found in the urine in cancerous ulceration of the bladder.

In all the forms of cystitis we find **pus-cells** in the urine.

When rupture and perforation of the bladder-wall has taken place matters of very various kinds may reach its interior. A pelvic abscess may yield pus, and ulcerating uterine carcinoma putrid detritus and cancer-cells, a rectal ulcer or fistula fæces, a dermoid cyst its characteristic contents, and so on.

The most common matters entering the bladder from without are **bacteria,** and less frequently **yeast-cells.** If the urine offers them suitable conditions for growth and they are not forthwith removed from the bladder, they proceed to multiply; micrococci and sarcinæ do so most readily, bacilli less frequently.

Children and others sometimes pass solid objects (such as pencils, hair-pins, straws, etc.) through the urethra into the bladder, and pieces

of catheters are occasionally broken off and lost in like manner. Now and then shot and bullets which have penetrated the surrounding parts are found loose in the bladder.

560. The causes which give rise to the formation of concretions in the kidney and its pelvis may also give rise to **concretions** within the bladder. As we pointed out in Arts. 531 and 532 acid and alkaline fermentations of the urine are frequently the cause of these deposits, in other cases the cause lies in the nature of the food taken. Not uncommonly however we are unable to detect any sufficient cause.

Very often indeed the basis of a vesical calculus is a concretion which has passed from the pelvis of the kidney into the bladder, or a foreign body introduced from without. On such a basis solid deposits are formed, usually of triple phosphate and acid phosphate of calcium. The foreign bodies in fact set up vesical inflammation and the products of this undergo alkaline decomposition. Deposits of uric acid and urates are much less common.

These deposits take the form of **gravel**, or of **stone**. The stone is usually single, and sometimes reaches a very large size.

A stone is usually spherical or ovoid, and may be smooth, nodular, tuberculated, rough, or even spiny. When more than one are present they are occasionally facetted or polyhedral. Some stones are hard, some soft and friable. They are often stratified or laminar, and made up of a number of different substances.

The presence of a stone generally causes inflammation of the bladder, occasionally ulceration and hæmorrhage. As it irritates the bladder it causes it to contract, and sometimes at the same time hinders its evacuation; in this way a stone often leads to hypertrophy of the bladder-wall. At times the stone lies in a diverticulum or sacculation of the bladder, and may there become impacted.

Vesical calculi are classified according to their composition.

(1) Uric-acid and uratic calculi. Pure uric-acid stones are generally small and hard, and of a yellow red or brown tint. Uratic stones (containing urates of ammonium and magnesium) are seldom pure. The superficial layers are usually composed of calcium oxalate and ammonium-magnesium (triple) phosphate.

(2) Phosphatic and calcareous calculi. These consist mainly of calcium phosphate, or of ammonium-magnesium phosphate. Stones consisting entirely of calcium carbonate are very rare. All these stones are white or grayish white. Triple-phosphate stones are soft and friable, the others are hard.

(3) Oxalatic calculi, consisting of calcium oxalate, are hard and spiny; they are brown in color.

(4) Cystine-calculi are soft brownish-yellow and waxy.

(5) Xanthine-calculi are red, with a smooth surface and earthy fracture.

561. Inflammation of the bladder or **cystitis** is in most cases caused by the presence of irritant matters in the urine (Arts. 558–560), whether

due to morbid admixture or to decomposition; it may also be a result of traumatic injury, or of irritant impurities in the blood.

Catarrhal cystitis is characterized by the occurrence of shed epithelium, pus-cells, mucus, and generally red blood-cells, in the urine. In recent cases the mucous membrane appears but little altered. When the secretion is purulent the membrane is covered with a film of pus, and is sometimes very much swollen. When hæmorrhage has occurred the surface is of a uniform gray tint, or mottled with gray black and reddish-brown patches. If the inflammation has extended to the submucous and muscular coats, so that these are infiltrated, the whole wall becomes more or less thickened. In extreme cases the serous or peritoneal surface may be stained with bloody or slaty-gray patches, and at length purulent or putrid exudations may make their appearance in the subperitoneal tissue (**pericystitis**) and on the peritoneum itself. This of course happens only in very intense suppurative or septic inflammations, such as are set up by septic (bacterial) decomposition of the contents of the bladder.

Certain irritants, such as cantharidin, lead from the outset of the affection to superficial sloughing of the epithelium, which becomes detached in the form of necrotic flakes and shreds. Such infective disorders as measles, scarlatina, typhoid, septicæmia, etc. are occasionally accompanied by superficial diphtheritic desquamations in the form of isolated yellowish patches; in other instances the exudation is croupous.

When the urine becomes ammoniacal and putrid the epithelial layers, the connective tissue of the mucosa and submucosa, and even the muscular coat may in parts become necrosed and ulcerated, and at length gangrenous and putrid. In this way ulceration, gangrene, and abscess of the bladder-wall are developed, and ultimately perforation may occur at one or more points, with the result of secondary suppuration and necrosis in the neighboring tissues.

In the severer forms of cystitis the mucous surface is frequently rough and sandy with incrusted salts, chiefly triple-phosphate.

As we have already pointed out (Art. 553) inflammation of the bladder may extend to the ureters and the kidney, especially when there is retention of urine ('surgical kidney').

In **chronic cystitis** fibrous hyperplasia of the coats of the bladder, with true hypertrophy of its muscular coat (Art. 563), is a common occurrence.

Tuberculosis of the bladder begins with the formation of gray nodules surrounded by a zone of hyperæmia; these enlarge and turn yellow, and sooner or later break down into ulcers. The ulcers have a cheesy infiltrated floor and their borders are hyperæmic. They increase in size by progressive marginal disintegration and by coalescence, and in this way are formed large sinuous ulcerations, involving a considerable part of the mucosa and submucosa. Vesical tuberculosis is usually accompanied by

tuberculosis of the pelvis of the kidney (Art. 550) or, in the male, of the genital apparatus: it is indeed probable that the process starts in some part of the latter system.

The mucous membrane of the urinary tract, and especially that of the bladder, frequently contains a number of small aggregations of lymphadenoid tissue, and in catarrhal cystitis these become perceptibly swollen. They then look very much like tubercles, especially when they are surrounded by a hyperæmic zone.

Long-continued engorgement of the vesical blood-vessels leads to varicose dilatations of the veins, chiefly those near the neck of the bladder. They are sometimes referred to as **vesical hæmorrhoids**, and now and then obstruct the evacuation of the bladder or give rise to hæmorrhage.

Amyloid degeneration of the vesical mucous membrane is not rare, but as a rule it is not apparent without the aid of the microscope. In very rare instances the amyloid deposits may lead to induration of the mucosa and submucosa.

References:—VIRCHOW, *Krankhafte Geschwülste* II.; EBSTEIN, *Ziemssen's Cyclop.* XV.; KLEBS, *Handb. d. path. Anat.* I.; MAAS, *Krankh. d. Blase* (*König's Handb. d. Chirurgie*); CHAVASSE, *Étude sur la tuberculose des organes urinaires* Paris 1872; VOISIN, *Tuberculose des organes génito-urinaires, Bulletin de la soc. anat. de Paris* XLIX. (1874); KIRMISSON, *Cystite, ibid.* L. (1875); DURAND, *Cystite chronique, ibid.* LII. (1877); STEINTHAL, *Virch. Arch.* vol. 100; DU CASAL, *Cystite chronique, Gaz. hebd. de méd.* 1877; W. ROBERTS, *Brit. Med. Journ.* 2, 1881; HARRISON, *Internat. encyclop. of surgery* VI. London 1886.

562. The commonest of the **tumors** of the bladder is the so-called '**villous cancer**' or vascular papillomatous **fibroma.** It consists of a number of long and slender villi or papillary growths, springing from a comparatively narrow base: each villus consists of a delicate stroma containing wide and thin-walled vessels and covered with stratified epithelium. The growth does not extend into the deeper layers of the mucous membrane, and sometimes attains the size of a small apple. It is single or multiple, and is usually situated towards the base of the bladder not far from the neck, so as sometimes to obstruct the channel during micturition. The vessels and the stroma being alike delicate and fragile, the tumor is very apt to bleed and may thus prove very dangerous to the patient. From time to time fragments of the villi are detached and passed with the urine. The growth is not malignant and should not be described as a 'cancer.'

Primary **carcinoma** of the bladder is a very rare growth; it occurs both in men and women and takes the form of a nodular or fungous or papillary tumor, at times extending over a considerable part of the bladder, and penetrating the submucous and even the muscular coat. The cancerous infiltration may thence extend into neighboring parts.

Secondary carcinoma is more frequently met with, the infection reaching the bladder from the uterus, vagina, rectum, or prostate.

Other neoplasms of the bladder are very rare indeed.

LANGHANS recently described a case of vesical angioma (*Virch. Arch.* vol. 86): GUSSENBAUER (*Arch. f. klin. Chir.* XVIII.) and VOLKMANN (*ibid.* XIX.) cases of myoma, SCHATZ (*Arch. f. Gynäk.* X.) of fibromyxoma, POSNER (*Berl. klin. Woch.* 1883) of primary carcinoma. See also STEIN, *Tumors of the bladder* Philadelphia 1881, *New York Med. Rec.* 1885 (with references to the recorded cases).

563. **Dilatation of the bladder** takes place when its evacuation is interfered with through occlusion or stricture of the urethra or paralysis of the muscular wall of the bladder itself. When the evacuation is rendered difficult, or when frequent contraction of the bladder is induced by the stimulus of a stone, the muscular coat may **hypertrophy.** The wall becomes thickened and the overgrown muscle-bundles stand out from the inner surface in a reticulum of bands or fasciculi.

Diverticuli are produced either by the simultaneous sacculation of all the coats, or by the protrusion of the mucous and submucous coats through the meshes of the fasciculated muscular coat. These diverticula are seldom larger than a walnut. They frequently are the seat of concretions, and sometimes are first caused by the pressure of a calculus.

Displacements of the bladder are rare, though occasionally a part of the viscus prolapses into a hernial sac. The base of the bladder may also fall down into the vagina (vaginal cystocele), or the posterior wall may prolapse through the dilated female urethra and appear at the external orifice.

Rupture of the bladder results from traumatic injury, excessive distention, or morbid change in the wall. Rupture into the peritoneum usually leads to fatal peritonitis. After perforations into the pelvic cellular tissue urinary infiltration takes place, leading to gangrene or suppuration in the tissue invaded. Ulceration or local necrosis sometimes leads to the opening of abnormal communications between the bladder and the vagina, uterus, rectum, or external cutaneous surface. These are called **urinary fistulæ,** and are kept open by the constant escape of urine through them.

CHAPTER LXXIV.

MORBID CHANGES IN THE URETHRA.

564. The **inflammations of the urethra** correspond generally with those of other mucous membranes. Croupous and diphtheritic inflammations are rare, but catarrh is very frequently met with. The most important form of catarrh is **gonorrhœa,** which is set up by a specific micrococcus (NEISSER, HAAB, MARTIN). The micrococcus is conveyed to the urethra in the secretion from another mucous membrane affected with gonorrhœa, and multiplying sets up an inflammation characterized by its purulent catarrhal exudation, which is yellowish or greenish-yellow and sometimes slightly blood-stained. The inflammation may extend from the urethra to other parts of the urinary tract and to the neighboring genital organs, and ultimately affect (by metastasis) remote regions like the joints, as in gonorrhœal rheumatism.

The inflammation may also extend in the urethra from the mucous to the submucous strata, and thence to the periurethral connective tissue and the lymphatics.

It usually ends in recovery, though in places it may lead to ulceration and abscess, to fibrous hyperplasia, corrugation and thickening of the mucous membrane, or cicatricial contraction. These are most common in chronic cases (**gleet,** *goutte militaire*).

Other forms of urethral inflammation are the soft chancre or **chancroid** (Art. 391), the **hard chancre** or initial sclerosis of syphilis (Art. 391), and lupous and tuberculous disease. Ulceration is frequent behind the site of strictures, and it readily extends to the urethra from prostatic ulcers. When the ulceration goes deeply fistulous tracts may be formed, leading to urinary infiltration of the surrounding tissue and ultimately to abscesses and permanent urinary fistulæ. In the male these fistulæ have sometimes a very irregular almost labyrinthine course, and open either on the exterior or into the rectum.

A not uncommon after-effect of chronic inflammation is the development of polypous and papillary growths, such as the **'cauliflower excrescences'** (*condylomata acuminata*) or 'caruncles' which appear round the orifice of the urethra in women.

Varices, resembling rectal hæmorrhoids, are sometimes formed at the site last-named in consequence of long-continued inflammatory hyperæmia.

The most common **tumors** affecting the female urethra are sarcoma, myxoma, fibroma, and carcinoma. Fibroma gives rise to nodes and nodules, or to vascular papillomatous growths. In males cancer of the prostate or of the glans penis frequently attacks the urethra. Small cysts of retention are occasionally formed in the mucous glands of the female urethra.

Stricture of the urethra is proximately due to inflammatory swelling of the mucous membrane, to nodular or diffuse unilateral or annular fibrous hyperplasia, to cicatrices, to valvular folds of membrane, or to polypus growths. Gonorrhœal inflammation and traumatic injury are the most common exciting causes. Inflammatory strictures are oftenest seated in the membranous and in the contiguous spongy part of the canal. In old men the **enlarged prostate** frequently obstructs and even occludes the urethra. In infants and young children the colliculus seminalis is sometimes so excessively developed as to interfere with micturition.

Traumatic rupture of the urethra arises in various ways; a very common cause is careless catheterization by which 'false passages' are produced. They are usually situate at the deeper end of the canal, and either end blindly or lead into the urethra again or into the bladder.

Such ruptures give rise to urinary infiltration and abscess, or to fistulæ surrounded by dense fibrous tissue and partially lined with epithelium.

References on the micrococcus of gonorrhœa (*gonococcus*):—NEISSER, *Cent. f. med. Wiss.* 28, 1879, *Deut. med. Woch.* 20, 1882; BOKAI, *Pest. med.-chir. Presse* 1880; CHEYNE, *Brit. Med. Journ.* 2, 1880; HAAB, *Corresp. f. Schweizer Aerzte* 1881, *Der Mikrokokkus d. Blenorrh. neonatorum* (*Horner's Festschrift* 1881); KRAUSE, *Cent. f. prakt. Augenheilk.* 1882; MARTIN, *Recherches sur les inflam. métast. suppur. à la suite de la gonorrhée* Geneva 1882; BOCKHART, *Vierteljahrsschr. f. Derm. u. Syph.* 1883; STERNBERG, *Philad. Med. News* 1883-84; WELANDER, *Gaz. méd. de Paris* 1884; LOMER, *Deut. med. Woch.* 1886.

CHAPTER LXXV.

MORBID CHANGES IN THE SUPRARENALS.

565. **Malformations** of the suprarenals are not common: though sometimes there are more than two or there are small accessory bodies of like structure; or on the other hand they are imperfectly developed or absent altogether. The latter is usually the case only when other malformations of the viscera are present.

Fatty degeneration is a normal phenomenon in the adult; it is apparent chiefly in the cells of the cortical layer, which thereby acquire a pale-yellow tint.

Amyloid change of the blood-vessels is not infrequent as an accompaniment of amyloid disease in other organs; it may give rise to induration.

Pigmentation is a very common occurrence in old age, affecting chiefly the deeper layers of the cortex. The cells are either of a uniform yellow tint or beset with pigment-granules.

Hæmorrhage is somewhat uncommon, though cases occur in which the extravasation is so great as to cause the organ to swell enormously. It is then due either to mechanical injury, or to vascular disorder. VIRCHOW describes an acute hæmorrhagic form of inflammation of the suprarenals.

Inflammation of the suprarenals is not frequently observed, though it does occur in various forms. Thus in acquired and in hereditary syphilis cellular infiltrations and gummatous inflammations are described. And in other cases inflammation ending in suppuration or in cicatricial induration has been noted.

The commonest as well as the most important variety of inflammation is that which terminates in **caseous and fibroid degeneration** of the gland: in most cases it is apparently of a tuberculous nature. The suprarenals are more or less enlarged, the capsule thickened and adherent to the neighboring structures. The surface is either smooth or nodular and mishappen: on section the parenchyma appears in great part replaced by dense fibrous tissue enclosing caseous foci of various sizes. These latter may contract or be absorbed, whereupon the organ becomes distorted and shrunken; in other instances they become calcified. The disease is usually bilateral. Sometimes abscesses are formed.

The **tumor** oftenest observed in the suprarenals is that described by

VIRCHOW as *struma lipomatosa suprarenalis:* it is a nodular growth consisting essentially of fatty glandular tissue. Carcinoma and sarcoma also occur, the latter often reaching a very large size.

Suprarenal **cysts** have also been described by various observers. They are formed either by the softening of hæmorrhagic patches, or by the dilatation of the cortical acini (KLEBS). These true cysts must not be confounded with the cavities very frequently observed in the glands, which are due to post-mortem softening of the inner layers of the cortex.

The *Echinococcus* is the only **animal parasite** met with in the suprarenals.

Disease of the suprarenals, especially the caseous fibroid degeneration, is often accompanied by **bronzing of the skin** (*cutis œnea*) and buccal mucous membrane, and by a profound and fatal cachexia. The pigmentation is sometimes uniform and diffuse, sometimes in patches and streaks. The bronzing and the cachexia are supposed to depend on the suprarenal lesion; the affection being referred to as *melasma suprarenale* or **Addison's disease.** In many cases changes in the abdominal sympathetic nerves and ganglia have been observed. No satisfactory explanation of the relation of the several phenomena has yet been given.

References:—ADDISON, *On the constitutional and local effects of disease of the suprarenal capsules* London 1855, reprint (New Syd. Soc., 1868); HECKER, *Monatsschr. f. Geburtskunde* XXXIII. (1869); VIRCHOW, *Krankh. Geschwülste* II.; KLEBS, *Path. Anat.* I.; AVERBECK, *Die Addison'sche Krankheit* Erlangen 1869; WOLF *Berl. klin. Woch.* 1869; GREENHOW, *Croonian lectures* London 1875, *Trans. Path. Soc.* (many papers), *Trans. inter. med. congress* II. London 1881; BURGER, *Die Nebenniere u. d. Morbus Addisonii* Berlin 1883; CHIARI, *Wien. med. Presse* XXI. (1880); FLEISCHER and PENZOLDT, *Deut. Arch. f. klin. Med.* XXVI. (1880); HUBER, *ibid.* IV.; GOODHART, *Atlas of Pathology* (New Syd. Soc.) London 1879, *Trans. Path. Soc.* XXXIII. 1882; DA COSTA and LONGSTRETH, *Amer. Journ. med. sciences* July 1880; SAUNDBY, *Brit. Med. Journ.* 1, 1883; BARLOW and COUPLAND, *Trans. Path. Soc.* XXXVI. 1885.

MARCHAND (*Virch. Arch.* vol. 92) has recently pointed out that accessory suprarenals are not uncommonly to be found in the broad ligament near the ovary. On suprarenal tissue in and about the kidney see Art. 556.

SECTION X.

THE RESPIRATORY ORGANS.

CHAPTER LXXVI.

INTRODUCTORY.

566. The **organs of respiration** fall naturally into two groups distinguished by differences both of structure and of function. The one includes the **lungs,** in which chemical interchanges between the blood and the air are effected; the other is the system of **air-passages** by which the lungs are placed in communication with the exterior.

The air-passages include the nose, larynx, trachea, and bronchi. From the point of view of morbid anatomy these are regarded simply as cavities lined with mucous membrane, and the morbid changes they undergo are conditioned chiefly by changes in this membrane. Certain parts of this system of passages perform functions other than that of air-conduction—for instance, the nasal mucous membrane contains the peripheral olfactory apparatus, and the larynx the mechanism of voice—but the fact affects but little the pathological relations of these parts. These functions involve the presence of certain structures in the epithelial wall of the air-passages, and these are sometimes secondarily (sometimes also primarily) affected when the latter is morbidly altered.

The general considerations set forth in Section VI. (Arts. 414–431), are accordingly in the main directly applicable to the case of the mucous membranes of the nose, larynx, trachea, and bronchi.

The pathological relations of the lungs themselves (*i. e.* of the respiratory tissues) are however of an essentially different kind. The peculiar structure of this part of the respiratory apparatus gives a special and peculiar character to its morbid anatomy and to the clinical course of the diseases affecting it.

The disorders of the respiratory organs are for the most part due to deleterious influences affecting their tissues through the medium of the respired air. The affections which are traceable to disturbances of the circulation or to alterations in the blood are however by no means insignificant. Affections due to extension of morbid processes from contiguous parts are comparatively infrequent.

CHAPTER LXXVII.

THE NASAL CAVITIES.

567. Congenital **malformations of the nose** which are at all extreme are met with only in combination with other malformations of the face. Thus in *Cyclopia* (Art. 7) the nose may be wanting or represented by a snout-like projection beneath the single orbit. Minor anomalies are—the absence of some of the nasal muscles, defects of the septum, of the ethmoid, or of the nasal bones, constriction or closure of the posterior nares, obliquity or distortion of the septum, and clefts of the alæ nasi or of the floor of the nostrils. The latter occur in connection with cleft-palate and cleft-face (Art. 8).

Hæmorrhage from the nasal mucous membrane (**epistaxis**) is very common, and may be due either to diapedesis or to rupture of blood-vessels. In many persons epistaxis is habitual: in others it occurs most frequently in connection with the hæmorrhagic diathesis, and in various infective diseases, menstrual disorders, venous engorgement, inflammatory conditions, etc.

Inflammation of the nasal mucous membrane (**rhinitis**) is one of the commonest affections. It usually takes the form of a mucous or purulent catarrh (Art. 420); the croupous, diphtheritic, phlegmonous, and ulcerative varieties are much less common.

Acute nasal catarrh is spoken of as **coryza,** and may result from a great variety of causes, such as cold, inhalation of irritant matters, micro-organisms, etc.

Chronic nasal catarrh occurs chiefly in persons who are scrofulous, phthisical, or syphilitic: it is comparatively rare in persons otherwise healthy. Sometimes it results in thickening, sometimes in thinning or even atrophy, of the mucous membrane. In the latter case the nasal cavity appears abnormally large, and its walls secrete a yellowish or greenish pus which undergoes putrid decomposition and gives rise to a fœtid odor (**ozæna** simplex) and to the formation of dirty greenish crusts and scales. FRÄNKEL points out that in this form of atrophy the Bowman's glands disappear, and it is very probable that the alteration in the nasal secretion thereby occasioned makes it possible for septic organisms to lodge in the mucous membrane. In many chronic cases the bone underlying the mucous membrane likewise undergoes atrophic change.

FRÄNKEL thus speaks of simple ozæna as *rhinitis chronica atrophica fœtida.*

Croupous and diphtheritic inflammation of the nose is usually secondary to the like affection in the throat (Arts. 423–426). Phlegmonous inflammation (Art. 427) is usually due to extension from neighboring parts, though it is sometimes confined to the nose.

Ulcerative inflammation is in most cases due to syphilis (Art. 429) or to glanders (Art. 430). Lupous (Art. 392), tuberculous (Art. 428), and leprous (Art. 430) infiltration and ulceration are also met with, but they are rare. The syphilitic and tuberculous affections of the nose frequently begin in the periosteum of the nasal bones and give rise to more or less extensive destruction of the osseous tissue.

All the inflammatory affections of the nose may extend by continuity to the cavities and sinuses connected with it and there take on a more or less independent character, the cavities becoming filled with mucous or purulent secretion. From the frontal or ethmoidal sinuses the inflammation may extend into the interior of the cranium and so give rise to meningitis.

References on ozæna:—HUPPERT, *Begriff und Ursachen der Ozæna* In. Diss. Strasburg 1879; B. FRÄNKEL, *Ziemssen's Cyclop.* IV.; MICHEL, *Krankh. d. Nasenhöhle und d. Nasenrachenraumes* Berlin 1876; E. FRÄNKEL, *Virch. Arch.* vols. 79, 87, 90; HARTMANN, *Deutsche med. Woch.* 13, 1878; GOTTSTEIN, *Breslauer ärztl. Zeitschr.* 17, 1879; KRAUSE, *Virch. Arch.* vol. 85, *Trans. internat. med. congress* III. London 1881; B. ROBINSON, *Nasal Catarrh* New York 1880; FRANKS, *Dublin Journ. med. science* 1881, 1882; MARTIN, *De l'ozène vrai* Thèse de Paris 1881; MORELL MACKENZIE, *Diseases of the throat and nose* II. London 1884 (with full references), LÖWENBERG, *Deut. med. Woch.* 1885.

References on nasal lupus:—HEBRA and KAPOSI, *Diseases of the skin* IV. (New Syd. Soc.) London 1875; MOINEL, *Le lupus scrofuleux des fosses nasales* Paris 1877.

References on nasal tuberculosis:—WEICHSELBAUM, *Allg. Wiener med. Zeitung* 27 and 28, 1881; TORNWALDT, *Deut. Arch. f. Ohrenheilk.* X., *Deut. Arch. f. klin. Med.* XXVII.; BRESGEN, *Der chron. Nasen- und Rachencatarrh* Vienna 1883; ZUCKERKANDL, *Norm. u. path. Anat. d. Nasenhöhle u. ihrer pneum. Anhänge* Vienna 1882; DEMME, *Berl. klin. Woch.* 1883 (states that tuberculosis may attack the nose primarily); VOLKMANN, *Samml. klin. Vorträge* 168, 169.

References on phlegmonous inflammation of the nasal cavities:—WEICHSELBAUM, *Wiener med. Jahrb.* 1881; KOHTS, *Gerhardt's Handb. d. Kinderkr.* III.; B. FRÄNKEL, *Ziemssen's Cyclop.* IV.

568. The nasal mucous membrane is not infrequently the seat of hyperplastic growths and of tumors, due partly to chronic inflammation, partly to unrecognized causes. They take the form of polypous excrescences and are usually referred to as **nasal polypi.**

Soft or mucous polypi resemble the mucous membrane in structure, but are somewhat more cellular. Sometimes the included mucous glands are dilated into cysts (cystic polypi) especially in the antrum of High-

more, or these glands are enlarged and multiplied as in glandular or adenomatous polypi, or traversed by numerous thin-walled blood-vessels (telangiectatic polypi or 'erectile' tumors).

Other polypi consist of œdematous connective tissue and mucoid tissue, and are therefore classed as fibromata and myxomata. They are more translucent than the former, and are usually of a yellowish tint, the mucous polypi being gray or grayish-red.

Sarcoma, dense fibroma, osteofibroma, chondroma, osteoma, carcinoma, and mixed tumors of the connective-tissue group, have been met with in the nose. Many of these start not in the mucous membrane but in the periosteum of the nasal bones. The connective-tissue tumors, especially those originating in the periosteum, may reach a considerable size, distending the cavity in which they grow, sometimes protruding from the anterior and posterior nares, and much distorting the face.

Carcinoma of the nose is most frequently met with about the anterior nares and is therefore to be classed with the cutaneous forms of cancer. The cancers which originate in the mucous membrane take the form of irregularly nodulated growths, which sooner or later ulcerate.

Rhinoliths are calcareous concretions, formed as a rule round some foreign body which has become impacted in the nasal cavity. In rare instances they are due to the inspissation of nasal secretions.

Maggots or larvæ are sometimes hatched in the nose from eggs deposited by various species of *Diptera*. They may give rise to extensive inflammation and sloughing. (See MORELL MACKENZIE, *Diseases of the throat and nose* II. London 1884.) Of **vegetable parasites** bacteria and the *Saccharomyces albicans* are the commonest. The former are usually innocuous, though in certain cases, as in ozæna, they set up decomposition in the nasal secretions. In tuberculosis and in glanders the characteristic bacilli are found.

References on nasal tumors:—VIRCHOW, *Krankhafte Geschwülste* I., III.; BILLROTH, *Ueber den Bau der Schleimpolypen* 1855; MATHIEU, *Les polypes muqueux* Thèse de Paris 1875; THUDICHUM, *Polypus in the nose* London 1877; DURHAM, *Holmes's Syst. of surgery* II. London 1883; KOHTS, *Gerhardt's Handb. d. Kinderkrankh.* III.; HOPMANN, *Virch. Arch.* vol. 93, *Wien. med. Presse* 1883; ZUCKERKANDL, *Norm. u. path. Anat. d. Nasenhöhle* Vienna 1882; LEFFERTS, *Internat. encyclop. of surgery* V. London 1885; MORELL MACKENZIE, *Diseases of the throat and nose* II. London 1884: the last two give many references to published cases.

CHAPTER LXXVIII.

THE LARYNX.

569. **Malformations.** Entire absence of the larynx is very rare as a congenital anomaly; it is met with only in amorphous and acephalous acardiac monsters in whom the lungs are undeveloped (Art. 13). Congenital defects, as of the epiglottis or of part or the whole of one of the laryngeal cartilages, are much commoner. Asymmetry and abnormal largeness or smallness of the larynx are also met with: abnormal smallness frequently accompanies aplasia of the testicle or early castration. Sometimes the laryngeal cartilages are abnormal in number, and the epiglottis more or less deeply cleft. The ventricles of the larynx or sinuses of Morgagni are not uncommonly of abnormally great capacity, and occasionally we find extra-laryngeal pouches communicating with them. This anomaly is of special interest, inasmuch as it is a normal feature in the *Quadrumana*.

Of acquired deformities **laryngeal stenosis** is the most noteworthy. It may be due to pressure from without, but more commonly to disease of the larynx; for example, to inflammation by which the mucous membrane becomes swollen and covered with a solid exudation or undergoes cicatricial contraction, or to the growth of intra-laryngeal tumors. Functional stenosis may be brought about by paralysis of the muscles which open the glottis or spasm of the muscles which close it. Foreign bodies impacted in the glottis may have the same effect.

The morbid anatomy of the larynx has been very thoroughly discussed by EPPINGER (*Klebs's Handb. d. path. Anat.* part 7 vol. II. Berlin 1880).

Numerous references to the pathology of laryngeal affections will be found in the following text-books:—RAUCHFUSS, *Gerhardt's Handb. d. Kinderkrankh.* III. Tübingen 1878; VON ZIEMSSEN, *Ziemssen's Cyclop.* IV., VII.; TÜRCK, *Klinik d. Krankheiten d. Kehlkopfes* Vienna 1866; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1884; P. BRUNS, *Die Laryngotomie* Berlin 1878; MORELL MACKENZIE, *Diseases of the throat and nose* I. London 1880.

570. **Affections of the laryngeal mucous membrane.** Laryngeal catarrh is very common, and is characterized by redness and swelling of the mucous membrane together with a mucous, purulent, or serous exudation. Serous exudation is observed chiefly in catarrhs due to persistent passive hyperæmia. The inflammation may extend over the entire

organ or be limited to certain parts such as the vocal cords or the epiglottis. It may be induced by very various causes.

In **chronic catarrh** the blood-vessels are sometimes permanently dilated. The epithelium desquamates freely and often accumulates round the vocal cords in whitish films and patches, which form a nidus for bacteria. The mucosa and submucosa are infiltrated with leucocytes. The fibrous strata frequently become hypertrophied and thickened. When the papillary structures of the glottis also are hypertrophied they assume the form of papillomatous or warty growths. The mucous glands of the posterior surface of the epiglottis, the false cords, and the sinuses of Morgagni may become enlarged and dilated, and give the surface a granulated appearance (**granular laryngitis**). Loss of epithelium and rupture of the dilated and extended glands give rise to small erosions and ulcerations. Loss of continuous patches of epithelium is most frequently observed about the vocal cords and their posterior attachments, and is often due to the action of bacteria or of the thrush-fungus (Fig. 76, Art. 198).

In chronic catarrh of long standing and in consequence of ulceration the glandular structures become obliterated and the mucous membrane thinned and atrophied. Slight but often-repeated irritation is sometimes followed by hypertrophy of the squamous epithelium, which gives the affected spots a white or pearly appearance. The vocal cords are the parts most commonly affected, and they are sometimes the seat of polypous excrescences at the same time (Art. 575).

Croupous inflammation of the laryngeal mucous membrane is sometimes primary, sometimes secondary to inflammation in neighboring parts. It is most common in connection with diphtheria, small-pox, typhoid, and cholera, though it may also result from the inhalation of hot or irritant gases and vapors or from the introduction of foreign bodies. The interior of the larynx is covered with white or yellowish more or less coherent false membranes or only with white curdy flakes; these are sometimes readily removed, sometimes slightly adherent. The latter is the case when the epithelium of the affected part is stratified and squamous (Arts. 423–426).

The false membranes consist in part of fibrinous filaments and meshes enclosing pus-corpuscles, in part of lustrous homogeneous flakes. When they are stripped off the underlying mucous membrane is red and raw-looking.

Diphtheritic inflammation with sloughing and gangrene of the mucous membrane occurs most frequently in connection with diphtheria and typhoid, though it is rare even in these diseases.

References:—EPPINGER, and RAUCHFUSS, *loc. cit.*; VON ZIEMSSEN and STEINER, *Ziemssen's Cyclop.* IV.; RHEINER, *Virch. Arch.* vol. 5; E. WAGNER, *Arch. d. Heilk.* VII. (1866); STEUDENER, *Virch. Arch.* vol. 54; WEIGERT, *ibid.* vol. 70; SCHOTTELIUS, *Gesellsch. d. Naturwissenschaften zu Marburg* XII.; Report, *Brit. Med. Journ.* 2.

1878; MORELL MACKENZIE, *op. cit.*, *Diphtheria* London, 1878: Report, *Lancet* 1, 1879, and *Med. chir. Trans.* LXII. (1879); MONTI, *Croup u. Diphtherie* Vienna 1884; VIRCHOW, *Berl. klin. Woch.* 1885; ORTH, *Path. Anat.* II. Berlin 1885.

It will be seen that we make no pathological distinction corresponding to that implied in the clinical terms *croup* and *diphtheria*. The specific infective disease diphtheria, when it is accompanied by croupous or superficial diphtheritic inflammation of the larynx and trachea, is the same as the affection clinically described as 'membranous croup,' a term which the pathologist may well dispense with (Arts. 204, 443, 444).

571. **Œdema of the glottis** is a more or less intense swelling of the laryngeal mucous membrane, due to infiltration of the mucosa and especially of the submucosa. The swelling is usually greatest on the posterior surface of the epiglottis, the aryteno-epiglottic folds, and the false vocal cords, the submucosa of these parts being exceptionally loose in texture. The œdema may be so great as to occlude the superior orifice of the larynx.

Œdema of the glottis may be acute or chronic. The former is due to inflammatory exudation, and occurs chiefly as a concomitant of catarrhal, croupous, or diphtheritic inflammation, and around syphilitic and tuberculous ulcers and submucous or perichondritic abscesses. It may also accompany suppurative inflammations of the pharynx, thyroid gland, and cervical connective tissue. It is often unilateral or confined to one of the parts above mentioned, according to the exciting cause.

Chronic œdema is usually the result of venous engorgement from cardiac disease, pulmonary emphysema, compression of the cervical veins, etc., and of non-inflammatory affections of the blood or vessels: it is generally symmetrical and limited to the posterior surface of the epiglottis and the aryteno-epiglottic folds, though in a less degree it may affect the vocal cords. Chronic inflammatory conditions of the larynx (as in laryngeal ulcer or perichondritis) may of course give rise to inflammatory œdema of a somewhat chronic kind.

Phlegmonous Inflammation of the larynx (*phlegmon laryngis*) is a sero-purulent and sero-fibrinous infiltration of the submucosa and mucosa, whose seat is generally the same as that of acute œdema: it is not common.

Suppuration of the tissue succeeds the infiltration, and abscesses are formed which on rupturing give rise to ulcers. When the inflammation extends to the cartilages purulent perichondritis is set up (Art. 576). These abscesses may also burrow in among the cervical muscles, or break into the pharynx or œsophagus. When the pus is evacuated the abscess-cavity may close up and become cicatrized.

Phlegmonous laryngitis sometimes follows upon croupous, diphtheritic, and gangrenous inflammations, and upon tuberculous and syphilitic ulcerations. In other cases inflammations of the perichondrium or of the pharynx or tonsils, or mechanical injury, are the inducing

cause. The forms of laryngitis which sometimes accompany typhoid, scarlatina, and pyæmia occasionally issue in suppuration.

572. **Specific forms of laryngitis.** We thus observe that the various forms of laryngeal inflammation result from very various causes, some of them being specific. Certain specific forms are distinguished by no definite characters from the non-specific; but there are others, notably those accompanying some of the infective diseases, which exhibit anatomical lesions more or less definite. The diseases in question are typhoid, small-pox, tuberculosis, syphilis, glanders, and lupus.

Typhoid is frequently accompanied by a catarrhal laryngitis marked by epithelial desquamation, ecchymoses, and superficial erosions, and by linear cracks in the mucous membrane, especially about the edges of the epiglottis. Sometimes the posterior surface of the epiglottis, the anterior wall of the larynx, and the vocal cords are covered with a branny slightly adherent 'fur' consisting of dead epithelium, leucocytes, micrococci, and microbacteria. Sometimes too on the false and true vocal cords there are ulcers, the floor and edges of which are beset with bacteria.

EPPINGER regards these bacteria as the specific organisms of typhoid, and thinks they are the cause of the epithelial necrosis and ulceration: he therefore describes the affection as *necrosis mycotica typhosa.* The bacteria are very probably the cause of the local destruction of tissue, but it seems highly doubtful that they are the virus of typhoid.

Different forms of bacteria are found in the affected spots, and the like changes are produced in affections other than typhoid (Fig. 76, Art. 198). It is therefore probable that different organisms are carried from the mouth, settle in the catarrhal mucous membrane, and there set up destructive changes.

Less frequently than the above we find in the larynx of typhoid patients diffuse swellings or miliary nodules, due to intense cellular infiltration of the mucous membrane. EPPINGER regards these as specific typhoid lesions analogous to those of the intestine. They occur chiefly at the base of the epiglottis, the false vocal cords, the inner aspect of the arytenoid cartilages, and the anterior attachment of the vocal cords: by disintegration of the infiltrated tissue they give rise to erosions with raised borders resembling typhoid ulcers. These ulcers, whether bacterial or infiltrated, may extend both in breadth and in depth, affecting ultimately the perichondrium of the several cartilages. In consequence of this we not infrequently observe large losses of substance with necrosis of the affected cartilages. The latter occurs chiefly when as sometimes happens the perichondritis becomes suppurative or gangrenous.

The laryngitis of **small-pox** is characterized by the appearance on the reddened mucous membrane of minute whitish spots or small lentil-like nodules. According to EPPINGER the former are due to cloudy

swelling and granular degeneration, the latter to cellular infiltration, of the epithelium. Sometimes a branny coating of dead epithelium and pus-corpuscles, or coherent croupous membranes, cover the affected parts. In all of these micrococci can be found (EPPINGER), and are probably the exciting cause of the local affection. Epithelial hæmorrhages make their appearance in cases of hæmorrhagic small-pox; and in the latter stages small abscesses may form in the connective tissue. Larger perichondritic abscesses and necrosis of cartilage are however comparatively rare.

Scarlatina gives rise to catarrhal laryngitis, seldom to the croupous or diphtheritic forms: and the like is true of measles and typhus.

References :—LOUIS, *La fièvre typhoïde* Paris 1841; TROUSSEAU, *Clinical Medicine* II. (New Syd. Soc.) London 1869: EPPINGER, *loc. cit.;* TOBOLD, *Laryngoscopie* Berlin 1874; HEINZE, *Die Kehlkopfsschwindsucht* Leipzig 1879; JOFFROY, *Arch. de physiol.* 1880; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1884; MURCHISON, *Continued fevers* London 1884; KÜHLE, *Sammlung klin. Vorträge* 6; GRAVES, *Clinical Lectures* (New Syd. Soc.) London 1884–85. **Erysipelas** may extend from the face and mouth to the pharynx and larynx, and give rise to œdematous and phlegmonous inflammation (CORNIL *Arch. générales* XIX. 1862; MORELL MACKENZIE, *op. cit.;* MASSEI, *D. primäre Erysipel d. Kehlkopfes* Berlin 1886).

573. **Tuberculous laryngitis** is a very common complication of tuberculous disease of the lung (laryngeal phthisis), though it also occurs independently. In the former case the specific infection is doubtless conveyed by the sputum; in other cases the virus reaches the mucous membrane by way of the blood or lymph.

The process begins with the development of small subepithelial cellular infiltrations, projecting somewhat above the surface as grayish nodules. These either caseate rapidly and breaking through the epithelium give rise to minute ulcerations, or extend beneath the surface in the form of a diffuse granulomatous infiltration containing typical tubercles and giving rise to irregular protuberances of the mucous membrane. Sooner or later caseation and disintegration set in, and ulcers are formed whose floor and margins are infiltrated or even caseous. Secondary changes presently appear in the form of disseminated patches of inflammatory infiltration in the mucosa, submucosa, or perichondrium, sometimes in the mucous glands or more rarely between the laryngeal muscles. These patches may also coalesce into larger masses of granulomatous tissue containing tubercles simple or caseous. This is most apt to happen about the perichondrium of the various cartilages.

Large tuberculous granulations are very commonly met with on the under surface and edges of the epiglottis, or on the posterior and anterior walls of the larynx. In the vocal cords on the other hand disintegration usually sets in before granulations of any size are developed. There is however no invariable rule in the matter: the extent of the tuberculous

infiltration and of the ensuing ulceration varies greatly in different cases. Sometimes there are only a few punctiform ulcers on the vocal cords or posterior laryngeal wall, in other cases large areas of mucous membrane are destroyed and the cartilages also are involved in the necrotic process.

Tuberculous ulceration is always accompanied by a certain amount of catarrh: œdema of the glottis or phlegmonous inflammation are also occasional complications.

References:—EPPINGER, *loc. cit.*; HEINZE, *Die Kehlkopfschwindsucht* Leipzig 1879; VON ZIEMSSEN, *Ziemssen's Cyclop.* VII., and supplement 1881; MORELL MACKENZIE, *op. cit.*, and *Brit. Med. Journ.* 1, 1879; BIEFEL, *D. Arch. f. klin. Med.* XXX. 1882; SOLIS COHEN, *Amer. Journ. med. sci.* 1883. HEINZE believes that the tuberculous metastasis from the lungs to the larynx takes place through the blood and not by means of the sputa. This is however very unlikely: the sputa from a tuberculous lung contain bacilli and are infective, they may therefore very well convey the specific infection to the larynx.

RINDFLEISCH affirms that the tuberculous ulceration starts from the mouths of the mucous glands. This may sometimes be the case, but it is not the rule.

574. The first symptoms of **syphilitic laryngitis** may be those of a simple catarrh, though the accompanying infiltration of the mucous membrane is often extreme. The affection usually follows upon syphilitic disease of the pharynx, and is doubtless an extension of the latter.

At a later stage deep erosions appear, whose floor and edges are densely infiltrated. Prominent grayish-white or red patches are formed on the surface of the mucous membrane (*condylomata lata, plaques muqueuses*), which also ulcerate as a rule; sometimes however the infiltration is re-absorbed and they disappear.

These erosions or ulcers vary much in extent and in depth. The floor of the larger ulcers is covered with a gray film: when this is removed the characteristic whitish exudation appears beneath. The epiglottis, the vocal cords, and the posterior wall of the larynx are the most frequent seats of ulceration. In rare cases the whole of the interior of the larynx is denuded and the cartilages laid bare.

A second form of syphilitic ulceration is due to the breaking down of gummata; these are usually seated in the submucosa and are not due to direct infection from the pharynx. They are most common in the epiglottis and vocal cords, and may be so large and numerous as to obstruct or occlude the larynx.

Small gummatous nodes may be re-absorbed, but the large ones usually soften in the centre and break through into the larynx, giving rise to flask-shaped ulcers with infiltrated edges. The ulceration may extend into the laryngeal wall and cause perichondritis and necrosis of cartilage: in this case the inflammation takes on a purulent or suppurative character.

The syphilitic process may come to a stand-still at any stage, the ulcers healing up by cicatrization. If the healing is delayed consider-

able portions of the larynx, such as the epiglottis or vocal cords, may be entirely destroyed. The greater the loss of substance the larger is the cicatrix, and the distortion of the parts due to its contraction may be extreme: sometimes indeed the cavity of the larynx is constricted to a narrow and tortuous passage. The vocal cords occasionally become adherent, or the glottis is encroached on by protuberant bands of scar-tissue.

The islands of mucous membrane lying between the cicatrices are often thrust or bulged out in the process, and if they become inflamed and infiltrated or hyperplastic they take the form of outgrowths and papillomatous or polypous excrescences (*condylomata acuminata*) which still further obstruct the air-passage.

Lupus of the larynx may accompany lupus of the pharynx and of the nose. It gives rise to nodular infiltrations and ulcers with a thickened edge and granulating floor, which yield a scanty secretion. Cicatricial contractions are formed, causing distortion and obstruction as in the case of syphilis.

Leprosy likewise gives rise to nodes and nodules in the larynx which coalesce into larger tumor-like growths. The subsequent ulceration, cicatrization, and cicatricial contraction may cause very great distortion of the parts.

In **glanders** disseminated inflammation is set up, which is characterized by the formation of subepithelial cellular nodules. These break down and ulcerate, and in this way extensive destruction of the mucous membrane takes place.

References:—EPPINGER, *loc. cit.*; VON ZIEMSSEN, *loc. cit.*; VIRCHOW, *Krankhafte Geschwülste* II.; GERHARDT and ROTH, *Virch. Arch.* vols. 20, 21; SOMMERBRODT, *Wiener med. Presse* 20, 1870, *Berl. klin. Woch.* 1878, *London Med. Record* 1878; TÜRCK, *Atlas d. Kehlkopfkrankheiten* Vienna 1866; SCHECH, *Deut. Arch. f. klin. Med.* XX., *D. Zeitschr. f. pract. Med.* 1877; WHISTLER, *Med. Times and Gaz.* 2, 1878; HAUFF, *Die Rotzkrankheiten beim Menschen* Stuttgart 1855 (glanders); BOLLINGER, *Ziemssen's Cyclop.* III., and supplement 1881; J. MACKENZIE, *Amer. Journ. med. sci.* 1880 (congenital syphilis), LEWIN, *Berl. klin. Woch.* 41, 1881; CHIARI and RIEHL, *Viertelj. f. Derm. u. Syph.* 1882 (lupus); THIN, *Brit. Med. Journ.* 2, 1884 (leprosy).

575. **Mucous polypi** of the larynx are not common; but now and then we meet with polypous thickenings of the false vocal cords, whose structure is exactly similar to that of the mucous membrane.

Papillary or villous growths are much more common and are described as **papillomata** or papillary fibromata. Some of them are of inflammatory origin, others appear to be non-inflammatory or simply hyperplastic. They generally grow from the true vocal cords and sometimes extend over a considerable area. They take the form either of compact nodulated tumors, or warty growths, or 'cauliflower' excrescences.

These latter are not infrequently multiple and are especially common in young persons (P. BRUNS).

Fibromatous nodules are also most frequently met with on the vocal cords. They have broad or narrow bases, and are smooth or warty, usually of the size of a lentil or small pea but sometimes as large as a hazel-nut. Some are pale, others vascular, some hard, others soft.

Lipoma and myxoma are very rare. Sarcoma is somewhat more frequent; it generally resembles a nodular fibroma, but is rather softer. Chondromata have been several times described: they start from the cartilages and form small knotty growths.

Primary **carcinoma** is most apt to arise about the vocal cords and the laryngeal sinuses. It takes the form of nodular or papillary growths or of diffuse infiltrations, which break down and leave sinuous ulcers with an irregular floor. The ulceration is usually accompanied by purulent inflammation. The destruction of tissue is sometimes very extensive, going far beyond the limits of the larynx.

Secondary cancerous growths are more common, extending into the larynx by continuity from the œsophagus, pharynx, or thyroid gland. True carcinomatous metastasis is somewhat rarer.

A few cases of adenoma have been noted; the growth takes the form of an irregular nodose tumor.

Cysts due to retention of secretion in the mucous glands are usually met with in the laryngeal sinuses and about the epiglottis; but they are not very common.

Of the **parasites** of the larynx other than the specific and other bacteria already mentioned we need only refer to the *Saccharomyces* or *Oïdium albicans* (Arts. 224, 436) or thrush-fungus, and the *Trichina spiralis* (Art. 232). The fungus gives rise to the characteristic white films; the *Trichina* lodges in the laryngeal muscles. Now and then round-worms (*Ascaris lumbricoides*, Art. 228) find their way into the glottis and give rise to attacks of dyspnœa.

References on laryngeal tumors:—EPPINGER, *loc. cit.*; VON ZIEMSSEN, *loc. cit.* (for recent bibliography by LEFFERTS see supplement London 1881); FAUVEL, *Traité d. maladies d. larynx* Paris 1877; VON BRUNS, *Neue Beobacht. üb. Kehlkopfpolypen* Tübingen 1873, 1878; OERTEL, *Deut. Arch. f. klin. Med.* XV.; MORELL MACKENZIE, *Growths in the larynx* London 1876, and *op. cit.*; BUROW, *Berl. klin. Woch.* 13, 1877, *Laryngoskopisch. Atlas* Stuttgart 1877; BESCHORNER, *Berl. klin. Woch.* 42, 1877; P. BRUNS, *Die Laryngotomie zur Entfernung intralaryngealer Neubildungen* Berlin 1877 (the latter and also VON ZIEMSSEN describe laryngeal tumors consisting of thyroid-gland tissue); ZIEGLER, *Virch. Arch.* vol. 65 (tumors consisting solely of amyloid substance); BUTLIN, *Malignant disease of the larynx* London 1883; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1884; ASCH, *New York Med. Journ.* 1884 (chondroma, with references); CERVELATO, *Lo Sperimentale* 1881 (cysts, with cases); SCHROETTER, *Monatschr. für Ohrenheilkunde* 1884 (lipoma).

According to P. BRUNS out of 1100 tumors of the larynx 602 were papillomata.

346 fibromata, 73 mucous polypi, and 27 cysts. 76 per cent of the tumors were situated on the true vocal cords or at their anterior attachment.

On round-worms in the larynx see KÜCHENMEISTER and ZÜRN (*Die Parasiten d. Menschen* Leipzig 1882), FÜRST (*Wien. med. Woch.* 1879), MOSLER (*Zeitschr. f. klin. Med.* VI. 1883).

576. The **laryngeal cartilages** are apt in old age to undergo certain degenerative changes which we may perhaps describe as physiological. These are fibrillation, partial solution, and transformation into spongy osseous tissue. The process corresponds in details to the metaplasia or pathological ossification of the other cartilages of the body. The spongy bone thus produced may afterwards be partially replaced by fatty myeloid tissue or marrow.

This softening and ossification also occurs as a morbid change at an earlier age, especially in cases of chronic laryngitis. The transformation into bone begins in the deeper parts of the cartilages and thence extends towards the surface.

Bile-pigment is deposited in the cartilages in cases of jaundice, and urates in gout.

The most important affection is however the inflammation of the perichondrium, referred to as **laryngeal perichondritis.** It is usually a secondary affection, occurring in connection with suppurative and ulcerative disease and with carcinoma, and is especially frequent in pyæmia, small-pox, typhus, and severe typhoid. Sometimes it originates in the decubital necroses met with in aged and debilitated bedridden patients at the posterior aspect of the cricoid cartilage (Art. 450), and due to the persistent pressure of the larynx on the vertebral column. Perichondritis may also be set up by mechanical violence.

The inflammation is usually purulent, but tuberculous, caseous, and indurative varieties are met with. It is nearly always localized to some part of the cartilaginous framework of the larynx, most commonly to parts of the cricoid and arytenoids. The accumulated exudation lying on the surface of the cartilage gives rise to more or less marked swelling of the parts, and presently portions of the cartilage become necrosed. When the perichondritic abscess bursts either outwards or inwards the dead sequestrum may be exfoliated and extruded. Abscesses bursting inwards usually give rise to inflammation of the bronchi and lungs, those which burst outwards to perilaryngeal suppuration.

After the abscess is evacuated and the dead cartilage removed the wound may heal by granulation and cicatrization. When the loss of substance is large much contraction and distortion ensue. Smaller defects are filled up with fibrous tissue, actual regeneration of the lost cartilage taking place only to a very slight extent. So too in fracture of the cartilages from external violence repair takes place by means of new formations of fibrous tissue not of cartilage.

Now and then cartilaginous excrescences, or **ecchondroses,** make

, and in cases where the cartilages have already become
s have been described. They are usually found about
, but are nearly always very small, not exceeding the
A few instances of still larger growths are however on

:—SCHOTTELIUS, *Die Kehlkopfknorpel* Wiesbaden 1879; TÜRCK. *loc.*
ER, *loc. cit.;* MORELL MACKENZIE, *Trans. Path. Soc.* XXII. (1871);
, *Deut. Arch. f. klin. Med.* XI.; BRIEGER, *Zeitschr. f. klin. Med.* III.;
irch. Arch. vol. 72; LITTEN, *ibid.* vol. 66; VON ZIEMSSEN, *Ziemssen's*
II.

CHAPTER LXXIX.

THE TRACHEA.

577. **Malformations** of the trachea are not common. In acephalous monsters it is sometimes absent, the larynx and the lungs being sometimes present, sometimes not. Occasionally we meet with cases of abnormally short trachea, and of atresia or narrowness of this or one of the main bronchi. As a result of imperfect separation of the air-passage from the alimentary canal we may have a persistent communication between the trachea and the œsophagus, usually a little above the bifurcation of the former. When the two ends of the communicating passage become closed, it is transformed into a mucous cyst lined with ciliated epithelium.

Not infrequently some of the rings of the trachea are wanting; and in other cases they are abnormally coherent, or subdivided, or multiplied. The bifurcation may take place at an abnormally high level, or the first branch of the right bronchus may arise directly from the trachea.

Lastly we may have persistent remnants of the branchial clefts opening into the trachea, giving rise to so-called cervical fistulæ (Art. 8). These have recently acquired considerable interest inasmuch as VOLKMANN has shown that they may be the starting point of carcinomatous growths.

Acquired **dilatations** of the trachea are not very common; though we occasionally meet with cylindrical, fusiform, or sacculate dilatations due probably to expiratory pressure, when expiration is obstructed and the tracheal wall more yielding than usual. Sacculate dilatations are commonly situated on the posterior aspect of the tube.

Stenosis of the trachea is in general caused by compression from without; more rarely it is due to structural changes, or to growths and tumors of the tube itself. Goitre and other tumors of the neck, peritracheal abscesses, and aneurysms of the aorta may be the cause of compression: cicatrices and other hyperplastic formations may give rise to obstruction from within.

Compression may be unilateral or bilateral. When it is very chronic it may induce atrophy of the cartilages (ROSE) or lead to their transformation into fibrous tissue: it is however worthy of remark that sometimes no degenerative change is observed even when the compression has been extreme.

Perforation of the trachea, apart from mechanical injury, is most frequently due to cancerous and sarcomatous ulceration of the œsophagus or thyroid gland, and to aortic aneurysm, peritracheal abscess, or suppurating lymphatic glands: it is much less commonly caused by ulceration within the trachea. In cases of aneurysm the thinned-out wall of the sack pushes in the inter-annular spaces; and this is observed also in the case of carcinomatous and sarcomatous and of goitrous tumors.

Foreign bodies which become impacted in the trachea in general speedily set up inflammation and ulceration.

Wounds of the trachea are repaired by cicatricial tissue: regeneration of cartilage takes place only to a very slight extent.

References:—EPPINGER, *loc. cit.*; CRUVEILHIER, *Traité de l'anat. path.* II.; GRUBER, *Virch. Arch.* vol. 47; VIRCHOW, *Krankhafte Geschwülste* III.; DEMME and FÜRST, *Gerhardt's Handb. d. Kinderkrankh.* III.; WEIL, *Deut. Arch. f. klin. Med.* XIV. (1873); ROSE, *Langenbeck's Arch. f. klin. Chir.* XXII.; RIEGEL, *Ziemssen's Cyclop.* IV.; ELDRIDGE, *Amer. Journ. med. sci.* 1879 (sacculations); SCHOTTELIUS, *Die Kehlkopfknorpel* Wiesbaden 1879 (repair of wounds); BRISTOWE, *St. Thomas's Hosp. Reports* III.; VOLKMANN, *Cent. f. d. med. Wiss.* 1882.

578. The **inflammations of the trachea** have few special features, and are frequently associated with inflammatory affections of the larynx. Catarrh is sometimes due to non-specific irritation, sometimes it is a complication of infective diseases such as measles, small-pox, whooping-cough, influenza, syphilis, etc. Laryngitis or bronchitis (Art. 579) usually accompanies this latter form. Croupous inflammation is most common in diphtheria, and is characterized by the formation of a white fibrinous false membrane. Diphtheritic denudation or ulceration of the mucous membrane is not common.

Miliary **tuberculosis** of the tracheal mucous membrane is rare. Chronic tuberculosis is more frequent: it gives rise to extensive subepithelial infiltrations, which afterwards break down and form ulcers of various sizes. Sometimes it extends to the deeper structures, laying bare and partially destroying (by perichondritis) the cartilaginous rings. In rare cases the greater part of the mucous membrane is destroyed by ulceration.

Syphilitic disease produces lesions resembling those of the larynx; indeed it frequently extends from the latter downwards; it may however appear in the trachea independently. In this case it is usually deep-seated, and is often associated with syphilis of the bronchi. The specific inflammation may give rise to extensive destruction of tissue, extending to the cartilaginous structures: the cicatrices which result often cause by their contraction very remarkable distortion and stenosis of the tube, which may be beset in every direction with coarse fibrous bands. The edges of the syphilitic ulcers are sometimes the seat of papillary excrescences partly covered with stratified squamous epithelium.

After tracheotomy **granulations** sometimes spring from the internal wound, and seriously obstruct the air-passage.

Primary **tumors** of the trachea are rare. Fibroma, sarcoma, chondroma, osteoma, adenoma, and carcinoma, have been observed. Secondary growths due to extension from the œsophagus or thyroid gland are more common.

Cysts arise from retention of secretion in the mucous glands. They are usually situated on the posterior wall and may be as large as a walnut: as a rule they protrude into the space between the trachea and the œsophagus. EPPINGER asserts that the mucous glands may become distended with air forced into them through their ducts.

References on tracheal syphilis:—GERHARDT, *Deut. Arch. f. klin. Med.* II., III. (1867); BEGER, *ibid.* XXIII.; MORELL MACKENZIE, *Trans. Path. Soc.* XXII. (1871), and *op. cit.*; RAUCHFUSS, *Gerhardt's Handb. f. Kinderkrankh.* III.; TÜRCK, *loc. cit.*; KOCH, *Langenbeck's Arch. f. klin. Chir.* XX.; BERGER, *Schmidt's Jahrbücher* 1881 (with a summary of the literature).

References on tracheal tumors:—ROKITANSKY, *Path. Anat.* IV. (Syd. Soc.) London 1852; STÖRCK, *Pitha u. Billroth's Handb. d. Chirurg.* III.; SCHRÖTTER, *Wien. med. Jahrb.* 1868, 1870; STEUDENER, *Virch. Arch.* vol. 42; SIMON, *ibid.* vol. 57; LANGHANS, *ibid.* vol. 53; VIERLING, *Deut. Arch. f. klin. Med.* XXI.; KOPP, *ibid.* XXXII.

CHAPTER LXXX.

THE BRONCHI.

579. The morbid changes affecting the larger bronchi in general correspond closely to those of the larynx and trachea. There are however certain peculiarities connected with them, arising partly from their anatomical structure and partly from their relation to the lungs.

Hyperæmia and **anæmia** of the bronchi have no very distinctive characters. We may however note that both in engorgement and in congestion the bronchial mucous membrane may appear of a very deep red or purple tint.

Hæmorrhage from the mucous membrane is not uncommon: it takes the form of small ecchymoses or of larger effusions which mingle with the bronchial secretion. These are due to disturbance of the circulation or to morbid changes in the vessels or tissues. In hæmophilia, whether congenital or acquired (purpura), and more rarely in catarrhal inflammations, the hæmorrhage may be much more considerable and may partially fill the bronchi, while extensive suffusions appear in the mucous membrane. When the menses are suppressed it is said that hæmorrhage from the bronchi sometimes occurs. The blood effused into the bronchi may be aspirated into the lung and simulate pulmonary hæmorrhage.

The commonest of all bronchial affections is **bronchitis.** In catarrhal bronchitis the secretion from the inflamed mucous membrane is mucous, serous, purulent, or mixed. The mucus so abundantly secreted in the acute stage comes partly from the lining epithelium, partly from the mucous glands of the bronchial wall. Little plugs of mucus (which sometimes simulate tubercules) may be seen protruding from the orifices of these glands. The cellular elements contained in the bronchial secretion are nearly all pus-corpuscles. Epithelial cells are never abundant, inasmuch as they do not readily desquamate and when they do they usually become mucoid and dissolve (Arts. 420, 421).

When the secretion is very abundant, serous, and containing few cellular elements, the affection has been called serous **bronchorrhœa**; when the secretion is more puriform **bronchoblennorrhœa.** Sometimes the secretion decomposes and becomes foul-smelling under the influence of septic micro-organisms, and we have then fœtid or **putrid bronchitis.** In all forms of bronchitis the mucous membrane is more or less densely

infiltrated with cells: this is most marked however in the purulent or putrid forms, in which the infiltration extends even to the peribronchial tissue. The causes of bronchitis are very numerous, some of them acting through the inspired air, some through the blood. Fœtid bronchitis is most frequently associated with dilatation of the bronchi (bronchiectasis) or with gangrene of the lung, but it also occurs independently of these.

Croupous bronchitis is usually an accompaniment of croupous tracheitis, and is almost always due to the specific virus of diphtheria: it may however be set up in other ways, as for example by the aspiration of liquid from the mouth. In croupous pneumonia there is always a certain amount of croupous inflammation of the smaller bronchi. The mucous membrane is covered over with whitish films whose thickness (except in croupous pneumonia) is not great in any but the larger bronchi: in the smaller tubes mere specks and shreds of fibrin are formed, and as we pass to the finest bronchioles these gradually disappear and are replaced by catarrhal secretion.

There is also a chronic fibrinous or **plastic bronchitis** in which

FIG. 216. TUBERCULOSIS OF THE BRONCHIAL MUCOUS MEMBRANE. (× 25)

a, columnar epithelium
b, fibrous tissue of the mucosa infiltrated with leucocytes
c, tubercle
d, margin of a small tuberculous ulcer

from time to time firm coherent membranes form in the bronchi, and are coughed up as continuous tree-like casts of the ramifying tubes.

Diphtheritic and **gangrenous inflammation** of the bronchial mucous membrane are rare. They are generally set up by gangrenous or necrotic detritus coughed up from the lung, or by powerfully irritant matters which have been inspired. The inflammation thus induced is sometimes hæmorrhagic, and patches of the mucous membrane and of the deeper structures of the bronchial wall become gangrenous and are thus destroyed.

Tuberculous inflammation of the bronchi is a common accompaniment of tuberculous disease of the lung. It is usually most marked in the smaller tubes communicating with the diseased region: in other cases it is diffused over the greater part of the bronchial system. Here as elsewhere the affection begins with the formation of gray cellular nodules (Fig. 216), which project somewhat above the surface. These caseate and break down, and in this way small ulcers (*d*) are formed, whose floor and edges are usually covered with a whitish necrotic film and surrounded by a zone of hyperæmia.

The disintegration of the infiltrated margins of the ulcer steadily advances, and the ulcer grows and coalesces with others, so that at length large irregularly-shaped erosions are formed which sometimes extend to the cartilages of the bronchial wall. In the smaller tubes we frequently find the entire wall invaded and ulcerated away.

Syphilitic inflammation of the bronchi is not often seen: it presents the same appearances as in the trachea and larynx. Extensive loss of substance is occasionally caused by it; as recovery takes place coarse puckered cicatrices are formed, and these may give rise to notable contraction and distortion of the bronchi.

The bronchi are provided with a stratified epithelium, consisting of flat basal cells, transitional cells, and columnar cells. Some of the latter are ciliated cylindrical cells, others are mucus-producing goblet-cells, which in catarrhal conditions undergo mucoid degeneration. The capillaries of the mucous membrane empty themselves chiefly into the pulmonary veins, not into the bronchial veins: to this fact is due the readiness with which the membrane becomes engorged when the pulmonary circulation is overloaded (KÜTTNER, *Virch. Arch.* vol. 73).

The tissue of the bronchial wall contains lymphoid elements, and in the larger bronchi these are in places aggregated into groups lying between the muscular coat and the cartilages: in this way lymphadenoid nodules are formed which look not unlike tubercles.

References:—FRANKENHÄUSER, *Bau der Tracheebronchialschleimhaut* St. Petersburg 1879; J. ARNOLD, *Virch. Arch.* vol. 80; KÖLLIKER, *Zur Kenntniss d. Baues d. Lunge* Würzburg 1881; ROSSBACH, *Ueber d. Schleimbildung in d. Luftwegen* (Festschrift) Würzburg 1882; RIEGEL, *Ziemssen's Cyclop.* IV.; WEIL, *Gerhardt's Handb. d. Kinderkrankh.* III.; SOKOLOFF, *Virch. Arch.* vol. 68; HAMILTON, *Path. of bronchitis* London 1883.

CURSCHMANN recently described (*Deut. Arch. f. klin. Med.* XXXII.) under the name of 'exudative bronchiolitis' a peculiar form of bronchitis in which tough hyaline or grayish or yellowish coagula are formed, 0.5–1 mm. thick and 1–2 cm. long, and consisting of spiral or convoluted filaments and strings enclosing a variable number of cells. They are due to an exudative process affecting the bronchioles, which is neither simple catarrh nor croupous inflammation. According to VIERORDT (*Berl. klin. Woch.* 1883) similar coagula are occasionally met with in other inflammatory affections, as in croupous pneumonia.

In various forms of bronchitis, but especially in the croupous and exudative varieties, the secretion contains slender acicular colorless octahedra of various sizes, which are known as Leyden's crystals: they are probably identical with Charcot's crystals (compare Art. 260), and seem to consist of some substance containing mucin (SALKOWSKI). Their occurrence is accidental, and it is possible that they are formed in or from lymphoid cells: they may form in the sputum after it has left the body (UNGAR).

References:—PEACOCK, *Trans. Path. Soc.* v. 1854; CHARCOT, *Gaz. hebdom.* 47, 1860; LEYDEN and SALKOWSKI, *Virch. Arch.* vol. 54; ZENKER, *Deut. Arch. f. klin. Med.* XVIII., XXXII.; CURSCHMANN, *loc. cit.*; UNGAR, *Cent. f. klin. Med.* 1880, *Congress f. innere Med.* Wiesbaden 1882; PRAMBERGER, *Ueber fibrinöse Bronchitis* Graz 1881.

580. **Stenosis** and **occlusion** of the bronchi are generally the result

of inflammation. When the bronchial wall is infiltrated and the mucous membrane covered with exudations and secretions, the air-passage is always to a certain extent obstructed, and some of the smaller bronchi are frequently blocked up entirely. As a rule this obstruction passes away, the morbid accumulations (mucus, pus, croupous exudations, etc.) being removed by absorption and expectoration, while the swelling of the bronchial wall gradually goes down.

Sometimes however the secretions are only imperfectly removed, and the obstruction persists for a considerable time. This is most frequently the case in the apices of the lungs, where the respiratory movements are less marked than in other parts. Secretions which are rich in cells or which become inspissated and viscid are apt to cause chronic obstruc-

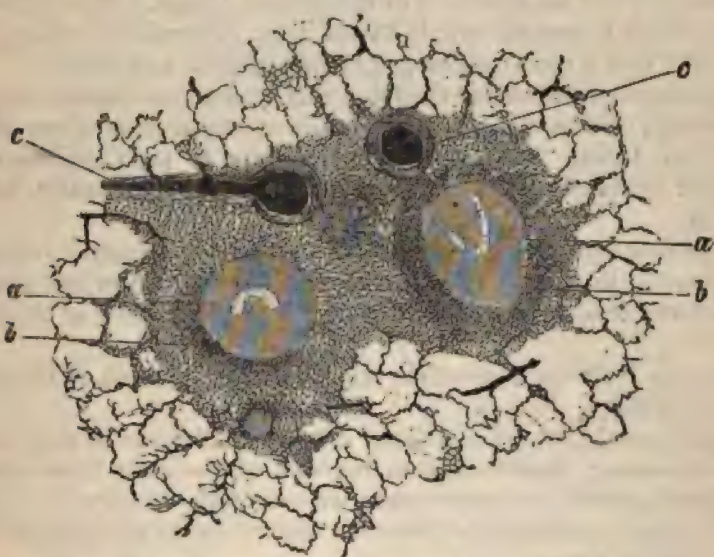


FIG. 217. TWO OCCLUDED BRONCHIOLES FROM A TUBERCULOUS LUNG.

(*Preparation injected with Prussian Blue, and stained with ammonia-carmine:* × 25.)

a, caseous contents of the bronchioles
b, bronchial wall and peribronchial tissue thickened and infiltrated with cells
c, arterioles

tion. Chronic thickening of the bronchial wall, whether from cellular infiltration or fibrous hyperplasia, has much the same effect.

Persistent obstruction of the bronchi may result from simple acute or chronic inflammation, but it is far more commonly due to tuberculous inflammation. This is owing to the fact that in tuberculosis we have not only thickening and infiltration of the bronchial wall but also a secretion which contains many cells and little liquid.

In chronic pulmonary tuberculosis the bronchi are always affected, and hence there are always a certain number of obstructed bronchioles

in the diseased region (Fig. 217): in many cases indeed most of the smaller tubes are occluded, and this fact contributes essentially to produce the characteristic appearance of the consolidated lung.

The contents of an occluded bronchus always become caseous (*a*), so that on section it looks like a round encapsulated caseous node. Only when a considerable length of the tube is filled with caseous detritus and when the section cuts it more or less longitudinally does it present the appearance of a cylindrical or elongated deposit. The boundary between the caseous contents and the bronchial wall is sometimes sharp and distinct, sometimes ill-defined. The former appearance is more characteristic of obstruction from catarrhal bronchitis, the latter of tuberculosis. The bronchus and the tissue around it are generally thickened in the neighborhood of the caseous deposit. The thickening after catarrh is oftenest simply fibroid, after tuberculous inflammation (Fig. 217 *b*) it is more cellular and in part necrotic and caseous.

The caseous contents of the tubes may after a time become calcified.

Foreign bodies also may by impaction cause obstruction of the bronchial tubes. They give rise, according to their chemical and physical character, to indurative, purulent, or it may be putrid, inflammation.

The cicatricial formations which follow upon destructive inflammation may by their contraction cause marked constriction and obstruction of the bronchi: this is well seen in syphilitic disease of the larger tubes.

In rare instances obstruction is caused by the growth of intrabronchial tumors.

Lastly, we may have stenosis by compression from pulmonary tumors or inflammatory growths, and at the root of the lung from enlarged lymphatic glands, aortic aneurysms, or œsophageal tumors.

For the consequences of bronchial obstruction as affecting the lung see Chapter LXXXIII.

581. **Hyperplasia and induration.** After long-enduring bronchial catarrh thickening and papillary overgrowth of the mucous membrane is sometimes though not frequently observed. The change is never extensive, and is of small importance.

The induration and thickening of the entire bronchial wall, which results from certain forms of inflammation, is much more important. The change is most frequently observed in the neighborhood of plugs of inspissated secretion, though it occurs also in unobstructed tubes and sometimes extends over a considerable number of their ramifications. It may also affect the peribronchial fibrous tissue and even extend to the contiguous parenchyma of the lung. From what we may call endobronchitis is developed indurative mesobronchitis and **peribronchitis** with peribronchial lymphangitis.

Indurative peribronchitis may also arise from the like change (cir-

rhosis) commencing in the lung, the process either being of the nature of direct extension or advancing from the bronchioles of the indurated parenchyma by way of the peribronchial lymphatics to the peribronchial fibrous tissue of the larger tubes. In like manner the inflammatory change may extend from inflammation of the pleuræ or of the interlobular septa. In rare instances the induration extends from the fibrous tissue

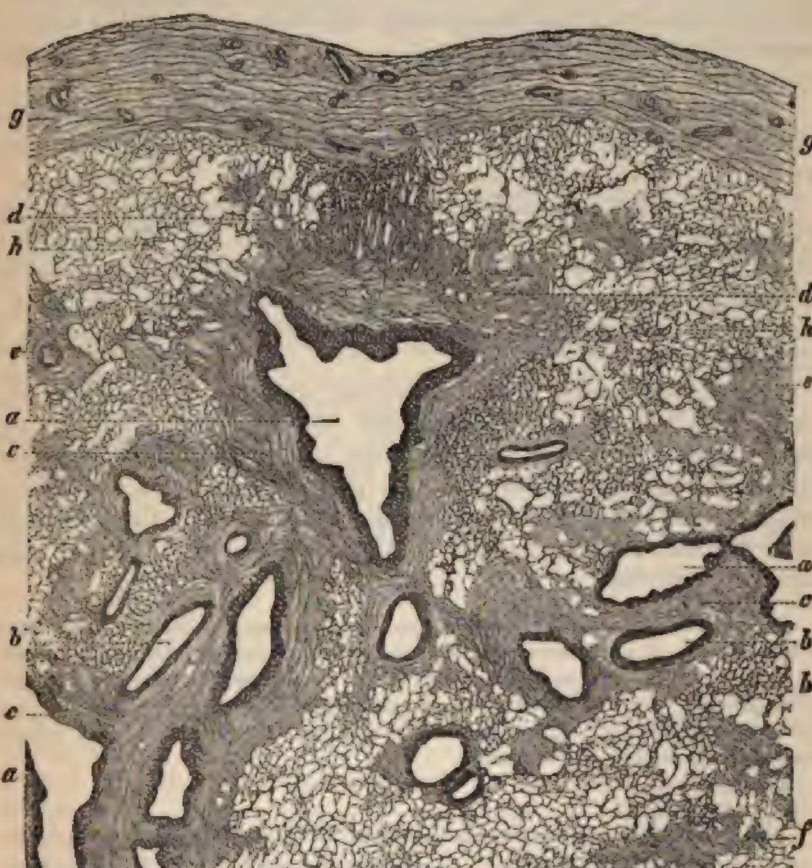


FIG. 218. INDURATIVE PERIBRONCHITIS.
(*Section stained with picrocarmine:* × 4.)

a, bronchi, some of them dilated
b, arteries
c, thickened peribronchial fibrous tissue
d, radiating bands of fibrous tissue
e, thickened bronchioles blocked up with secretion
f, fibroid indurations in which the bronchi have not been cut across
g, thickened pleura
h, pulmonary tissue, partly emphysematous

and lymphatic glands at the root of the lung, and proceeds radially along the peribronchial structures.

The appearance of a bronchus thus thickened and indurated varies

greatly according to the way in which the process has been set up. If the tube is unobstructed (Fig. 218) it looks on section like a thick-walled aperture, sharply defined against the pulmonary tissue or surrounded by radiating fibrous bands (*d*), and projecting above the cut surface. If the tube is filled with inspissated secretion (Fig. 218 *e*, Fig. 217 *a*), the wall looks like a thickened capsule surrounding it. When the adjacent parenchyma of the lung is devoid of air, collapsed (Fig. 218 *e*) and indurated, there is no sharp line between the thickened bronchus and the altered lung: a slight difference in tint and in consistence is all that appears.

Inflammations issuing in suppuration or in caseation extend to the peribronchial tissues and lymphatics in the same way as the indurative variety: they often extend both widely and deeply.

In tuberculous bronchopneumonia with caseation caseous peribronchitis is always present, and in suppuration of the lung there is always a certain amount of purulent peribronchial lymphangitis. Of course the tubes immediately connected with the seat of disease in the lung are the first and most affected, but the process often spreads to the bronchi of other regions.

Peribronchitis being thus a secondary affection, and usually associated with bronchitic and pneumonic processes, it is always accompanied by changes in the lung or in the pleura (Fig. 218 *g*). Indeed these latter changes are frequently the most apparent, and overshadow to a great extent the peribronchial lesions (Art. 614). Cases however occur in which these are so marked that they form the essential character of the disease.

The term peribronchitis is used in the text in a much more restricted sense than is usual. Most writers include under it the nodular indurations of bronchopneumonia. It is thought best however to distinguish between the finer terminal or respiratory bronchioles, and those which serve simply as air-passages. The former are essentially elements of the parenchyma of the lung, and their inflammations are essentially pneumonic.

For references see Art. 582.

582. **Bronchiectasis** or dilatation of the bronchi results partly from increased internal pressure on the bronchial wall, partly from changes in its structure and in that of the surrounding pulmonary tissue.

The dilatation is either uniform and extending over one or more branches, or local and fusiform or saccular: it may be single or multiple. Frequently we meet with several varieties of dilatation in the same patient.

Most frequently the dilatation is due to long-standing inflammatory affections by which the strength and elasticity of the bronchial wall is considerably diminished, so that it yields to the internal pressure of the respired air. Such dilatations are usually cylindrical, and are most marked in the lower lobes. When the wall yields unequally, the dilated

tube appears sacculated, and its inner surface is irregularly corrugated with annular, oblique, or reticulate ridges and bands. These are simply the circular fasciculi of the bronchial wall, which retain to some extent their form in spite of the dilatation, the mucous membrane bulging and yielding between them. The mucous membrane is moreover more or less atrophied and infiltrated, the cartilages are often partially disintegrated and replaced by fibrous tissue, and the orifices of the mucous glands are dilated into small funnels. The epithelium is sometimes little altered; but in other instances it is seen that the columnar cells have become mucoid or detached, so that the surface is lined only with short cubical or club-shaped cells devoid of cilia. This is especially the case where there is much catarrh.

Bronchiectasis is especially apt to occur when the branches of an inflamed bronchus are partially impermeable to air, so that the corresponding portion of the lung is collapsed and functionless. The result is that on inspiration the air entering the bronchus is not uniformly distributed; and even if the neighboring portions of the lung should dilate by way of compensation, as the thorax expands the air which rushes in is still unequally distributed and bears abnormally on the obstructed tube. Adhesions and thickenings of the pleura and of the interlobular fibrous tissue have often a like effect, inasmuch as they interfere with the equable expansion of the lung, and lead to irregularities in its distribution within the bronchi. Partial atelectasis (Art. 591) persisting after birth acts in the same way. When the pulmonary tissue round a bronchus undergoes contraction, it may in certain circumstances exercise traction on the bronchial wall and cause it to dilate. Lastly, when the bronchial secretion accumulates abnormally in an obstructed tube, it may give rise to considerable distention and dilatation.

The bronchiectases brought about in the ways just enumerated are seldom fusiform or cylindrical. They are often saccular, globular, or irregular in form, or arranged in a moniliform series. Sometimes in an indurated lung they are so numerous that the latter appears excavated in all directions. In very rare instances we meet with regular cysts filled with mucus, behind a bronchial obstruction.

In these dilatations the mucous membrane undergoes changes similar to those just described.

Papillary outgrowths are very rarely met with. The exterior layers of the bronchial wall, and the peribronchial fibrous tissue, are frequently much thickened, especially where there is inflammatory induration or cirrhosis of the lung. These are sometimes distinguished as hypertrophic bronchiectases.

References:—CORRIGAN, *Dublin Med. Journ.* 1838; BIERMER, *Virchow's Handb. d. spec. Path.* v., *Virch. Arch.* vol. 19; BUHL, *Lungenentzündung, Tuberculose und Schwindsucht* Munich 1872; LEBERT, *Klinik d. Brustkrankheiten* I.; TROJANOWSKY, *Beiträge z. Lehre von d. Bronchiectasie* In. Diss. 1864; FITZ, Virch.

[illegible] *Ziemssen's Cyclop.* IX.; LICHTHEIM, *Arch. f. exp. Path.* [illegible] *de Paris* 1878; LEROY, *Arch. de physiol.* 1879; [illegible] *Path. Hist.* II. London 1884; RIEGEL, *Ziemssen's* [illegible] *Path. of bronchitis* London 1883; HELLER, *D. Arch. f.* [illegible]

[illegible] RIEGEL, RINDFLEISCH) state that in bronchiectasis [illegible] and the muscular coat frequently become hypertrophied [illegible], but this ZIEGLER has not been able to verify. The [illegible] observed are not of new formation, but are simply [illegible] which have not yielded to the dilating forces.

[illegible] **Ulceration and perforation** of the bronchial wall is due [illegible] of the internal surface or to ulcerative affections [illegible] tissues. Purulent, putrid, and tuberculous inflam[illegible] apt to lead to ulceration and perforation from [illegible].

[illegible] is especially likely to occur when septic matters are in[illegible] air or when the bronchial secretion undergoes [illegible]. The latter takes place in bronchiectases, where [illegible] linger for a considerable time.

[illegible] occurs and the originating inflammation extends [illegible] parts, the peribronchial tissue and the adjacent lung[illegible], and according to the character of the inflamma[illegible] or suppurative and putrid disintegration. Caseous [illegible] thus issues in caseous or purulent peribronchitis, [illegible] becomes an ulcerated **bronchiectatic vomica.** The [illegible] either lies beside the primary dilatation or sur[illegible] or less completely.

[illegible] of the bronchial wall is at first usually partial, but [illegible] complete; and the bronchus then appears to open into [illegible] the cavity.

[illegible] of the cavity may appear gangrenous, caseous, or infil[illegible], according to the mode in which it has arisen and [illegible] at which the examination is made. Its liquid contents [illegible], or mixed with fragments of caseous detritus. The [illegible] contains bacteria, and often spherules of leucin and needles [illegible] and margarin.

[illegible] usually increases in size, and that most rapidly when the [illegible] suppurative or gangrenous; less rapidly when caseation takes [illegible] rapidly when the lung is already indurated by chronic [illegible]. The destructive process may advance not only peri[illegible] but also along the course of the peribronchial lymphatics: in [illegible] suppurative and caseous peribronchitis are not infrequently [illegible]

[illegible] and perforation of the bronchi from without are associ[illegible] with suppuration, gangrene, and caseation of the parenchyma of [illegible]: they are extremely common. Caseous or suppurating lymph-

atic glands, peribronchial tumors, and aneurysms, occasionally break through the bronchial wall.

When a bronchus is thus perforated the broken-down tissues and detritus pass into its lumen and are either coughed up or aspirated into other parts of the lung. Air on the other hand may enter the excavation from the bronchus.

On the **tumors** of the bronchi see Art. 619.

CHAPTER LXXXI.

STRUCTURE AND FUNCTION OF THE LUNGS.

584. The **parenchyma of the lung** is composed essentially of the terminal bronchioles and alveoli and of blood-vessels, together with a certain amount of connective tissue which unites the ultimate branches of the bronchi into lobules and marks them off one from another.

The transition from the air-tubes to the respiratory parenchyma is very gradual, the bronchial walls changing in structure by slow degrees and ultimately becoming sacculated. The bronchi subdivide dichoto-

FIG. 219. TERMINATION OF A BRONCHIOLE AND OF A PULMONARY ARTERIOLE.

(Prepared by corrosion: magnified by a hand-lens.)

A, bronchiole *B*, pulmonary arteriole

mously into ever finer branches, and it is the finest terminal branches or bronchioles which go to form the respiratory parenchyma. At first the sacculations or **alveoli** occur singly (Fig. 219 *B*), and then in small groups on one side of the bronchiole. The tubes which are thus partially transformed into respiratory tissue are known as **respiratory bronchioles.** Each respiratory bronchiole divides into two or three smaller branches, which are surrounded on all sides by alveoli (*B*) and

are known as **alveolar ducts.** The terminal alveoli are called **infundibula.**

As the smaller bronchi pass into the respiratory bronchioles they alter notably in structure. The cartilages disappear, and the epithelium is reduced to a single layer of low non-ciliated cells, which ultimately take the form of broad polygonal pavement cells (KÖLLIKER).

As the respiratory bronchiole changes to an alveolar duct these modified columnar cells in turn disappear, and the epithelium takes the form of small nucleated granular-looking pavement cells interspersed with larger hyaline plates some with and some without nuclei. The muscular fibres of the bronchioles persist as annular bands surrounding the orifices of the lateral alveoli and of the terminal infundibula.

The epithelium of the alveoli is like that of the alveolar ducts. Their walls consist of a delicate membrane strengthened by scattered

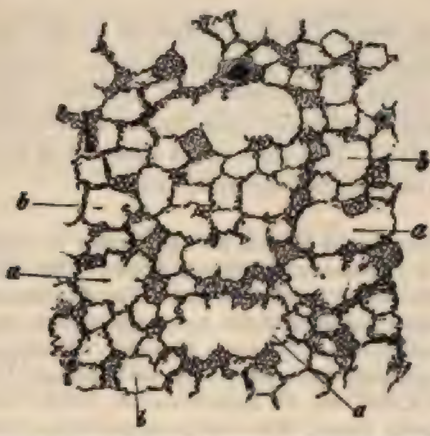


FIG. 220. SECTION OF AN INJECTED HEALTHY LUNG (× 20).

a, longitudinal, *b*, transverse sections of respiratory bronchioles, alveolar ducts, and infundibula.

filaments and bundles of elastic tissue. They are devoid of muscular fibres.

The clustered alveoli belonging to each bronchiole are not quite contiguous, but are separated by spaces which are filled by other groups of alveoli and infundibula. The contiguous groups are bound together by connective tissue.

In preparations made by maceration or corrosion the alveolar ducts of each bronchiole appear thus to stand apart from each other; while in sections (Fig. 220) the alveolar tissue looks like a continuous meshwork, interspersed with transverse and longitudinal sections (*a*, *b*) of bronchioles, alveolar ducts, and infundibula. At the boundaries of the several bronchiolar systems we find broader bands of connective tissue marking off the so-called **lobules.**

The pulmonary parenchyma derives its blood-supply almost entirely from the **pulmonary artery.** Its capillaries surround the walls of each air-cell or alveolus (Fig. 220), and their loops project into its cavity covered only by the thin epithelial lining. The terminal branches of each arteriole are not distributed to a single bronchiolar system only (Fig. 219 *A*), but supply several contiguous systems: they anastomose freely with the branches of neighboring arterioles (Fig. 220) and form a continuous network of vessels. The blood from the capillaries is collected into **interlobular veins** which run between the several arterial areas.

The **lymphatics** arise in clefts and spaces lying in the interalveolar septa. The radicles unite and run in the peribronchial and circumvascular tissue, or in the interlobular, subpleural, and pleural connective tissue. Both bronchi and arteries are very richly supplied with lymphatics.

Throughout the whole lymphatic system of the lung we meet with collections of lymphoid cells (FRIEDLÄNDER, ARNOLD, KÖLLIKER), which are either round or fusiform. In children these lymphadenoid patches contain large numbers of cells, but in adults they are often more fibrous and pigmented. The pigment is enclosed in round, fusiform, or stellate cells, or it may lie free between them.

References:—Text-books of normal histology such as *Quain's Anatomy* II. London 1882, KLEIN'S *Elements of Histology* London 1883; FRIEDLÄNDER, *Virch. Arch.* vol. 68; ARNOLD, *ibid.* vol. 80; KÖLLIKER, *Zur Kenntniss d. Baues d. Lunge* Würzburg 1881; KLEIN, *Anatomy of the lymphatic system* London 1875; FEUERSTÄK, *Ueber d. Verhalten d. Epithels bei d. fibrinösen Pneumonie* Göttingen 1882; KÜTTNER, *Die Kreislaufsverhältnisse d. Säugethierlunge, Virch. Arch.* vol. 73; COHNHEIM and LITTEN, *ibid.* vol. 65; ZUCKERKANDL, *Ueber Verbind. zwischen den art. Gefässen d. menschl. Lunge, Wiener Sitzungsberichte* LXXXVII.

The pulmonary artery is distributed almost entirely to the parenchyma of the lung, but it also according to KÜTTNER gives off small branches to the subpleural and interlobular connective tissue and to the bronchial mucous membrane. The pulmonary arterioles are terminal, but by dilatation of the communicating capillaries connections between neighboring arterial territories are readily established and perform the function of anastomoses.

The branches of the bronchial arteries subdivide with the bronchi and supply these and their nerves and lymphatic trunks. Their capillaries are connected with those of the pulmonary artery. The vessels which reach the lung from the mediastinal pleura supply the subpleural and interlobular lymphatics, but they also communicate with the pulmonary and bronchial arterial systems.

585. The **morbid affections** of the lung originate in the vascular system or in the bronchi, or are extensions by contiguity from neighboring parts.

The affections starting in the vascular system, that is to say depending on disturbance of the circulation or disorder of the blood, make their first appearance in small patches corresponding to the territory of

an arteriole, or they at once extend over a whole lobe, or over one or both lungs. In each case the extent and distribution of the local change is independent of the disposition and configuration of the smaller air-tubes.

With regard to affections of bronchial origin it must be noted that mere disturbance of the influx or efflux of respired air may give rise to grave changes in the pulmonary parenchyma. Impurity of the respired air is a still more potent cause of disease, as it leads not merely to morbid deposits in the lung but also, and very frequently, to inflammatory change. This latter is always at first localized, and often over areas corresponding precisely to the distribution of the bronchioles.

Disease of parts contiguous to the lung, and especially of the pleura, often give rise to pulmonary injury by the hindrance or obstruction of the respiration which they cause. In other cases the morbid process itself extends from the surrounding tissues to the lung, and usually spreads along the course of the lymphatic channels.

Malformations of the lung are on the whole not common. Absence of one or both lungs only occurs in cases where there are other grave defects of development. Absence of parts, abnormal smallness, etc., are met with in connection with malformation or deformity of the thorax. A small accessory lung unconnected with the trachea has once or twice been observed.

The commonest anomaly, and one which has no functional significance, is multiplication of the lobes.

In some of the lobes or in parts of them the air-tubes are occasionally absent or ill-developed, and then the corresponding part of the parenchyma consists simply of continuous cellular and highly vascular fibrous tissue. The bronchi leading to the airless tissue may be more or less dilated (Art. 582).

On the other hand we sometimes find in one or more parts of the lung large vesicular cavities resembling excessively distended alveoli.

On congenital malformations of the lungs see FÜRST (*Gerhardt's Handb. d. Kinderkrankheit.* III.), ROKITANSKY (*Path. Anat.* IV. (Syd. Soc.) London 1852), MAYLARD and L. HUMPHRY (*Journ. of Anat. and Physiol.* 1885), EDWARDS (*Amer. Jour. med. sci.* 1885).

CHAPTER LXXXII.

DISORDERS OF CIRCULATION IN THE LUNG.

586. **Congestive hyperæmia** may be due to diminution of the normal resistances to the arterial current within the lung, and may be induced by direct stimuli reaching the lung through the respired air, as when irritating or irrespirable gases are breathed or when the air is excessively hot or excessively cold. It is also the first step to inflammation. Partial or collateral congestion of one part of the lung sometimes results from obstruction of an important arterial branch in another part.

Congestion of the lung, when it is not collateral or due to local textural or vascular change (as in inflammation), extends uniformly over the whole organ. It is usually transient, and is very seldom fatal. In the fatal form of congestion called vascular **pulmonary apoplexy**, the lung appears swollen and abnormally firm, of a uniform dark-red color on section, and containing but little air; the capillaries are everywhere distended with blood and encroach on the alveolar cavities. There are usually some scattered extravasations of blood.

Engorgement or passive hyperæmia results from hindrance or obstruction to the outflow of blood through the pulmonary veins, or from causes tending to weaken the propelling forces. The latter appear when the activity of the right heart is impaired, when the pulmonary artery or its branches are obstructed, or when the respiration is interfered with. Thus when (as in suffocation) the inspiratory muscles dilate the thorax while air is prevented from entering the lungs, blood is as it were pumped from the extra-thoracic vessels into the intra-thoracic, and the blood collects and stagnates as it does under a cupping-glass.

Obstruction to the outflow of blood from the lung is most frequently caused by valvular lesions of the left heart; but the same effect is also indirectly produced by obstructive increase of pressure within the aorta which the heart is at length unable to overcome, and by relaxation or degeneration of the wall of the left ventricle.

Failure of the propulsive power of the heart causes engorgement chiefly of the dependent parts of the lung (**hypostatic engorgement**): arterial obstruction causes hyperæmia of the region supplied by the artery (Art. 589), and interference with respiration causes hyperæmia of

the lobules which are prevented from acting (Art. 591). When the engorgement is great the affected parts become purple or livid in color.

Passive hyperæmia may give rise to various secondary changes, such as hæmorrhage, œdema, dilatation of vessels, and loss of epithelium.

Anæmia of the lung may be due to general anæmia. When it is partial it is usually dependent on compression or excessive inflation of the part. After death the blood generally flows from the anterior portions of the lung to the deeper and posterior portions.

587. When in consequence of endocarditis and valvular thrombosis the mitral orifice is rapidly obstructed and the valve rendered incompetent, the backward pressure and consequent engorgement in the pulmonary veins is apt to be very great, and œdema, hæmorrhage, and epithelial desquamation ensue.

The **œdema** is marked by the escape of serous liquid into the alveoli (Art. 588), but in this variety the quantity of liquid is seldom great. The extravasation of blood also is not usually considerable, though there are here and there small hæmorrhages recognizable even with the unaided eye: the extravasated blood may fill the alveoli to the exclusion of air.

The epithelial desquamation is sometimes slight, but in other cases it is so abundant that the alveoli are all but filled with granular or homogeneous epithelial plates. The lung then looks grayish-red, and is abnormally firm to the touch: it contains little air, and in places may be entirely airless. The desquamation of epithelium is due to the transudation of lymph from the capillaries.

Mitral disease of long standing, when accompanied by hypertrophy of the right ventricle and permanent increase of pressure within the pulmonary vessels, leads to the condition known as **brown induration** of the lung. The organ is larger and firmer than usual, it contains less air, and its tissue is brownish-red and dry, or rarely œdematous. It often contains scattered hæmorrhagic patches and spots of brown.

The principal changes are dilatation of the vessels and pigmentation of the tissues. The dilatation is most marked in the capillaries, which protrude into and encroach on the alveolar spaces.

The **pigmentation** of the lung is due to the presence of yellow and brown granules deposited chiefly along the course of the lymphatics in the peribronchial, circumvascular, and interlobular tissues, and also to some extent in the alveolar walls. The granules are enclosed in stellate, fusiform, or rounded cells or lie free in the tissues. The alveolar epithelium is here and there pigmented.

The pigment is derived from the blood. When blood escapes from the vessels the alveoli are at first more or less filled with it. Part of it passes directly into the lymphatics which communicate with the lumen of the alveoli. Another portion disintegrates within the alveoli, and at the same time white blood-cells migrate from the capillaries and take up the disintegrated matters, becoming thus transformed into corpuscle-

carrying and pigment-granule cells. These lie at first within the alveoli and are sometimes met with in great numbers. Thence they may pass into the bronchi and are coughed up, but the greater number pass into the lymphatics and so reach the lymphatic glands, or remain lodged in the tissues of the lung, especially in the patches of lymphadenoid tissue. The detritus of the blood which passes directly into the lymphatics lodges in the same parts; the ultimate form which it takes being in all cases that of brown or even black pigment.

When the engorgement and excessive pressure persist for a long time the walls of the pulmonary vessels become hypertrophied, and the connective tissue is also somewhat increased. According to RINDFLEISCH and others the muscular fibres of the bronchi and alveolar ducts are also hypertrophied.

References:—DITTRICH, *Beitr. z. path. Anat. d. Lungenkrankheiten* Erlangen 1850; VIRCHOW, *Virch. Arch.* vol. 1; ZENKER, *Beitr. z. norm. u. path. Anat. d. Lungen* Dresden 1862; BUHL, *Virch. Arch.* vol. 16; RINDFLEISCH, *Path. Hist.* II. London 1873; HERTZ, *Ziemssen's Cyclop.* V.; ORTH, *Virch. Arch.* vol. 58; EBERTH, *ibid.* vol. 72.

588. **Œdema** of the lung is a condition in which the alveoli and bronchioles, and often the bronchi also, are filled with serous liquid more or less mingled with air. The condition may extend over the whole lung, or only over a lobe or part of a lobe. The pulmonary tissue may be either anæmic or hyperæmic.

Pulmonary œdema arises in various ways. It generally appears *in articulo mortis* as a result of the gradual failure of the heart. According to COHNHEIM it occurs when the outflow through the pulmonary veins is opposed by an obstruction that the right ventricle cannot overcome. This is the case when from weakness or excessive aortic resistance the left ventricle fails to empty itself in systole. COHNHEIM's explanation is based on experiment and no doubt applies to many cases of ante-mortem œdema, but not to all.

Not infrequently the signs of previous engorgement are entirely absent, and the distribution of the œdema is so irregular that we cannot refer it to a condition (like engorgement) extending over the whole lung. In such cases we must assume that we have to do with some alteration of the vessel-walls that causes them to be abnormally permeable, and is referable to the disease from which the patient has suffered. The like explanation will apply to the œdema which occasionally results from the breathing of irrespirable gases.

Another variety is the inflammatory œdema which generally accompanies certain inflammatory processes, such as croupous or suppurative inflammation. Lastly, multiple fat-embolism of the pulmonary arterioles may give rise to œdema from obstruction of the capillary circulation.

The liquid of pulmonary œdema is always albuminous, and usually poor in cellular elements derived from the blood. The œdema of engorgement not rarely is due to liquid which contains red blood-cells, often in such abundance as to give it a hæmorrhagic appearance.

Epithelial cells are sometimes abundant in the liquid, sometimes scanty: they are more or less swollen up. If catarrh is present at the same time, numbers of white blood-cells mingle with the liquid. Where pigmentation of the lung is in process some of these cells contain pigment-granules.

References:—COHNHEIM, *Allg. Path.* I. Berlin 1882; WELCH, *Virch. Arch.* vol. 72; POSNER, *ibid.* vol. 79; FALK, *ibid.* vol. 91; S. MAYER, *Wiener Sitzungsber.* LXXVII. 1878. *Prager med. Woch.* 14, 1880; LITTEN, *Berl. klin. Woch.* 1882.

589. **Hæmorrhage** from the pulmonary vessels is of very common occurrence and arises from a great variety of causes.

In the first place hæmorrhage is very frequently a result of engorgement, especially that due to violent inspiratory efforts with obstructed access of air (inspiratory dyspnœa). The quantity of blood which escapes is not usually so great as to cause firm hæmorrhagic infarction, but it may lead to the formation of rather large dark-brown patches of infiltrated and airless tissue.

When a large quantity of serous liquid transudes with the red blood-cells we have what is called hæmorrhagic œdema of the lung.

When the air is entirely displaced from the lung-tissue, so that it becomes dark-red and not unlike a soft and very vascular spleen, the condition has been termed **splenization** of the lung. It is most commonly a result of gradual cardiac paralysis before death: the blood no longer efficiently propelled accumulates in the deeper parts of the lung and so gives rise to what we might describe as hypostatic hæmorrhagic œdema. If as often happens inflammation begins in the engorged region the process is termed **hypostatic pneumonia.**

Extravasation of blood is an exceedingly common accompaniment of pneumonic and bronchopneumonic affections (Arts. 602, 613).

In acute inflammations the red blood-cells escape from the vessels with the inflammatory exudation, of which indeed they form a component part. In the later stages of the inflammation, when the pulmonary tissue breaks down, hæmorrhage is usually due to the rupture of small or large blood-vessels whose walls have been softened or ulcerated through.

In the case of the larger arterial branches the wall usually yields and becomes dilated into a small **aneurysm** before actual rupture. These aneurysms are most frequently observed on vessels which traverse or lie in the wall of ulcerating cavities. When they rupture more or less copious hæmorrhage ensues, and the cavities together with the bronchi which open into them are flooded with blood.

Mechanical injury, like that caused by a bullet or a broken rib, gives rise to bleeding whose amount depends of course on the nature and extent of the wound.

In somewhat rare cases pulmonary hæmorrhage is referable to a congenital or acquired hæmorrhagic diathesis, as in hæmophilia, in purpura, or in scurvy; or to infective diseases like scarlatina, typhoid, and small-pox; or lastly to cerebral disease, especially such as causes disturbance of the respiratory function. In the latter case the bleeding may be very considerable, whole segments of the lung becoming infiltrated and airless.

The most marked form of **hæmorrhagic infiltration** or **infarction** is that which follows thrombosis or embolism of a branch of the pulmonary artery. The infarct is usually subpleural, of a sharply defined conical form, and in the recent state dark brownish-red in color and firm in consistence. When the blood is somewhat leukæmic the infarct may be grayish-red or grayish-white in color. The emboli come from the right side of the heart or from the systemic veins and usually lodge at the bifurcation of the arterial branches. The characteristic extravasation takes place when the blood reaching the embolized region from the neighboring capillaries is insufficient to maintain the circulation.

Pulmonary infarcts vary in size from that of a cherry-stone to that of a hen's egg, though occasionally they are much larger. The pleura over a recent infarct is smooth and glistening, but afterwards it becomes turbid and covered with a thin fibrinous film.

Embolism of a pulmonary arteriole is not always followed by hæmorrhagic infarction, though the arteries are *terminal* in COHNHEIM'S sense of the word (Art. 30). Sometimes of course death ensues before there is time for the formation of an infarct, but apart from this the circulation may be maintained by the free influx of blood from the neighboring capillaries.

References on hæmorrhagic infarction of the lung:—VIRCHOW, *Gesammelte Abhandl.* Frankfort 1856; COHNHEIM, *Allg. Path.* I. Berlin 1882; PANUM, *Virch. Arch.* vol. 25; WILLIGK, *Prager Vierteljahrsschrift* L.; GERHARDT, *Sammlung klinischer Vorträge* 91, *Gerhardt's Handb. d. Kinderkrankh.* III.; HAMILTON, *Liverpool med. chir. Journ.* 5, 1883; LITTEN, *Berl. klin. Woch.* 1882.

References on pulmonary hæmorrhage in cerebral disease:—PINEL, *De l'hémorrhagie pulmonaire en rapport avec les lésions du cerveau* Thèse de Paris 1876; NOTHNAGEL, *Cent. f. d. med. Wiss.* 1874; JEHN, *ibid.*; BROWN SÉQUARD, *Lancet* 1, 1871; CHARCOT, *Leçons sur les maladies du syst. nerv.* Paris 1875; CARRÉ, *Archives générales* 1877.

590. Blood extravasated into the tissue of the lung is re-absorbed provided the tissue remains otherwise uninjured (Art. 587). The corpuscles dissolve and are taken up in solution, or they break up and pass, either free or enclosed in cells, into the lymphatics. Thence they are carried to the lymphatic glands, or are deposited in the walls of the lymphatic vessels, and give rise to black or brown pigmentation. Some of the cells containing disintegrated blood are removed with the sputum.

During the stage at which the lymphatics and the alveoli contain a large amount of disintegrated blood the pulmonary tissue has a dirty orange or rusty tint.

In more copious hæmorrhage, such as follows the rupture of an artery, blood passes into the bronchi and is coughed up (**hæmoptysis** or hæmoptoë). Some of the blood may be aspirated from the bronchi into neighboring branches and into their alveoli. In this way hæmorrhagic patches exactly resembling primary hæmorrhages are formed; usually however their number and distribution, and the circumstances in which they occur, enable us to discern their nature.

The firm hæmorrhagic infarct becomes rapidly decolorized, assuming a reddish-brown or rusty tint. Then a reactive inflammatory immigration of leucocytes sets in from the vessels of the contiguous parts, and accelerates the re-absorption of the blood. In the course of time such infarcts often disappear entirely, leaving no permanent structural change behind. In other cases the affected region is indicated by a more or less marked but seldom very definite condensation of the pulmonary tissue, with some cicatricial contraction; the pleural surface of the region is slightly drawn in, and shows a certain amount of fibroid thickening with white radiating bands extending from it. The condensed tissue is sometimes brown or slate-colored, sometimes undistinguishable in color from the surrounding tissue. The condensation is due partly to collapse of the infiltrated alveoli, partly to new-formation of fibrous tissue in the alveolar septa by which they are thickened and bound together into a compacter mass.

The embolus is meanwhile absorbed in like manner, its place being indicated by slight corrugations of the wall or filaments traversing the lumen of the artery.

When the infarct is large or the re-absorption of the extravasated blood and the re-establishment of the circulation delayed, part of the infiltrated tissue may perish and break down into an inodorous brownish-red pulp: this either makes its way into a bronchus and is so removed, or is re-absorbed. The loss of substance is repaired by the development of cicatricial tissue, provided no septic change is set up within the cavity.

In rare instances the re-absorption of blood and disintegrated lung-tissue is incomplete, and the detritus remaining passive for a time becomes thickened and caseous, and at length calcified, the whole being enclosed in a capsule of new-formed fibrous tissue.

When the embolus causing the infarction contains at the same time infective matters capable of setting up decomposition or suppuration, or when these reach the injured tissue with the inspired air, we may have gangrene or suppuration of the lung (Art. 605).

CHAPTER LXXXIII.

ATELECTASIS, COLLAPSE, AND EMPHYSEMA OF THE LUNG.

591. In the unborn child the lung is a compact structure, the alveoli exist potentially, but they are everywhere collapsed and airless. When respiration commences the alveoli become distended with air into hollow vesicles and the epithelial lining of their walls becomes expanded and flattened.

If the respiration is imperfect owing to the occlusion of a bronchus or the compression of some part of the lung, some of the lobules remain unexpanded and retain the dense fleshy consistence and livid tint of the fœtal organ. This condition is known as **fœtal atelectasis** or **apneumatosis.**

When a part of the lung which has once acted becomes from any cause airless it is said to be **collapsed** or atelectatic. The condition may be due to compression, or to obstruction of a bronchus. Compression of the lung is most commonly brought about by the collection of air or liquid in the pleural cavity, or by excessive elevation of the diaphragm: it may also be due to aortic aneurysm, spinal curvature, thickening and contraction of the pleura, distention of the pericardium, etc. The compression may be partial or total, and the collapse may be more or less complete.

When the collapse affects the whole lung and is complete, the organ is usually squeezed up against the spine, and its tissue is dense, tough, and airless: its color is generally pale pink or gray. Collapsed segments of the lung have a similar appearance, but there is often more blood in the part and so it has a redder color.

When a bronchus or bronchiole is occluded by secretion or other cause, the corresponding segment always becomes airless after a time. LICHTHEIM states that the oxygen of the enclosed air is first absorbed by the blood, then the carbonic acid, and ultimately the nitrogen; the lung shrinking to its fœtal condition.

As the collapsed part no longer expands or contracts with respiration, and its capillaries are much folded and contorted, a certain amount of engorgement takes place. The unexpanded tissue thus looks somewhat livid in tint, and is retracted or sunken in comparison with the normal tissue.

Obstructive collapse is extremely common and is indeed a usual accom-

paniment of inflammation of the smaller bronchi. *Post mortem* the lung looks mottled with livid retracted patches alternating with pink or reddish-white air-containing regions.

References:—WEBER, *Beiträge z. path. Anat. d. Neugebornen* Kiel 1852; BARTELS, *Virch. Arch.* vol. 21; HERTZ, *Ziemssen's Cyclop.* V.; GERHARDT, *Virch. Arch.* vol. 11, and *Gerhardt's Handb. d. Kinderkrankh.* III.; LICHTHEIM, *Arch. f. exp. Path.* X.; TRAUBE, *Gesamm. Beiträge z. Physiol. u. Path.* Berlin 1871; BALZER, *Gaz. méd. de Paris* 1878; ROMELAERE, *De l'atélectasie pulmonaire* Brussels 1881; SCHUCHART, *Virch. Arch.* vol. 101.

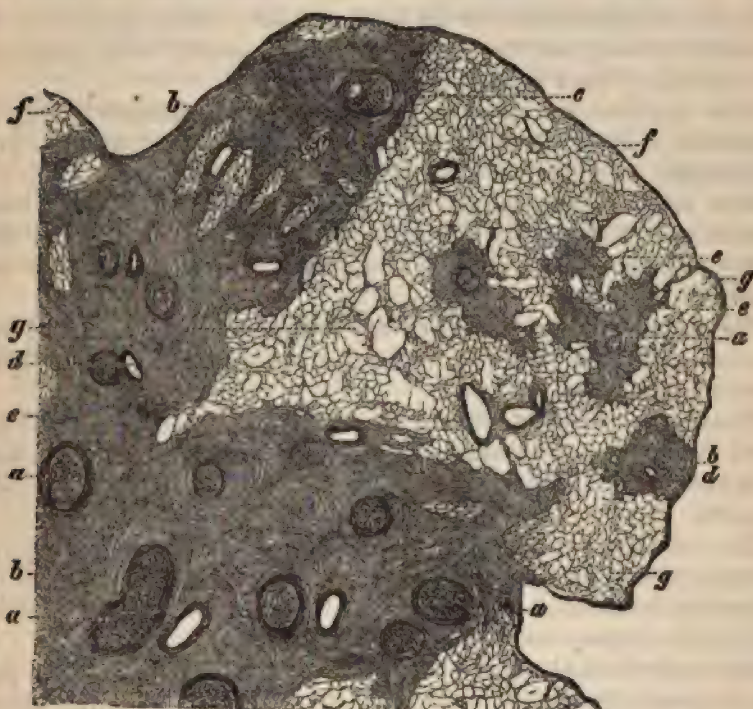


FIG. 221. CIRRHOSIS FROM COLLAPSE OF THE PULMONARY TISSUE.

(*Horizontal section through the apex of the lung, stained with picrocarmine and mounted in Canada balsam*: × 5.)

a, bronchi plugged with secretion
b, obliterated bronchioles
c, small bronchus distended with secretion
d, pulmonary arterioles
e, collapsed indurated pulmonary tissue
f, normal, *g*, emphysematous pulmonary tissue

592. **Results of collapse.** When a part of the lung remains collapsed for some time certain changes in its tissues usually make their appearance. Small hæmorrhages take place from the engorged vessels, by which the tissue becomes permeated by blood-cells and to some extent pigmented: it is however beyond doubt that much of the black pigment

which is ultimately deposited in the collapsed tissue is simply dust and carbonaceous matter inhaled before the bronchi became occluded. Presently the alveolar septa cohere and coalesce, and the tissue is transformed into a more or less compact and continuous mass (**carnification**).

The cohesion of the alveolar walls and the consequent condensation and induration of the tissue probably never take place without some slight inflammation, which is either conducted from the inflamed bronchi or set up by the extravasated blood. After a time but few remnants of pulmonary structure can be made out in the collapsed region, and in them the septa are thickened, the few shrunken alveoli are filled with cells, and the epithelium for the most part lost. Other parts (Fig. 221 *e*) consist of dense and compact fibrous tissue, usually much pigmented and resembling black india-rubber.

This condition we may call the **cirrhosis of collapse**: from the pigmentation which is always present it is often referred to as **gray induration.**

It is most common about the apex of the lung (Fig. 221), where catarrhal obstruction of the bronchi (*a*) frequently takes place and leads to the collapse of the corresponding alveoli with the changes just described.

The occluded bronchi are often hypertrophied (*a*) and distended with the accumulated secretion (*c*). The small respiratory bronchioles (*b*) are nearly all obliterated.

The surface of the condensed portion is always shrunken and distorted, and there are generally adhesions between the pleural surfaces which show that at some time or other inflammation has existed about the parts.

The pulmonary tissue lying between the collapsed regions is partly normal (*f*), partly emphysematous (*g*); it often includes small islands of collapsed and indurated tissue (*e*). The bronchi which are still pervious to air are not infrequently dilated (Art. 582).

When part of the lung persists in a state of fœtal atelectasis, the pulmonary tissue is by degrees transformed into compact unpigmented fibrous tissue, sometimes interspersed (HELLER, FEUSTEL) with bits of cartilage and adipose tissue, the obliterated alveoli being represented by a few clusters of epithelial cells. The corresponding bronchi are in general somewhat dilated, so that the unpigmented tissue is traversed by smooth-walled channels and cavities of various sizes: in particular instances these may be as large as a hen's egg. The cavities are lined with cylindrical epithelium, and like other bronchiectases may be the seat of inflammatory change.

HELLER (*Naturforscherversammlung in Freiburg* 1883, *D. Arch. f. klin. Med.* XXXVI. 1885) and FEUSTEL (*Ueber die späteren Schicksale der Atelektase* In. Diss. Kiel 1883) have recently directed attention to the bronchiectasis which may follow upon fœtal atelectasis. ZIEGLER has met with a typical example in the case of a

man of 35, in whom about a quarter of the upper lobe of the left lung was transformed into dense white fibrous tissue, excavated in all directions by smooth-walled cavities lined with cylindrical epithelium and communicating with bronchi. The largest cavity was about as large as a hen's egg. There were no signs whatever of any previous inflammation.

593. When the thorax is over-distended by forced inspiration, or when one part of the lung is pervious to air while another part is shut off, the pervious parts become excessively inflated and a condition which we may describe as **acute vesicular emphysema** is induced. The alveoli are not altered in structure but are simply over-distended. This condition is very commonly the result of bronchopneumonia. The distended lobules are pale and anæmic, and those that lie immediately beneath the pleura project like little blebs above the level of the normal or atelectatic parts.

When the pressure within an alveolus exceeds a certain amount its wall gives way, and air enters the interalveolar tissue and especially the lymphatic channels. This condition is called **intervesicular emphysema.** It is generally a result of bronchitis or bronchopneumonia accompanied by violent coughing, and is met with in children who have died of asphyxia during the course of these affections. It has also occurred from over-energetic attempts to insufflate the lungs of stillborn infants.

The alveoli of the anterior border of the upper lobe are the most apt to give way. The inflated vesicles are usually subpleural and may be as large as a pea. Sometimes air passes from them under the pleura towards the root of the lung and into the mediastinal adipose tissue, sometimes even inflating the subcutaneous structures of the neck and thorax (**subcutaneous emphysema**).

594. When the alveoli are subjected to persistent or often-repeated distention, partial atrophy and yielding of their walls ensue, and two or more alveoli being thus converted into one the pulmonary tissue is to that extent 'rarefied.' This state is called **chronic vesicular emphysema** or simply emphysema. Its production may be facilitated by disorders of nutrition, such for example as accompany local inflammation or senile decay. The lungs of many persons seem also normally to possess but little power of resistance to over-distention.

The atrophy of the septa begins at the point where they are thinnest, and first appears in the widening of the intercapillary spaces (Fig. 222 *a*) and the yielding or disappearance (*b*) of the elastic fibres. Holes and gaps next appear between the capillaries in the septa; they are at first very small (*b*), but soon enlarge (*d*). The over-stretched capillaries become impervious (*c*) and ultimately give way (*d*).

By the gradual extension of this process many of the septa and their capillaries at length disappear, the thicker fibrous bundles which surround the alveolar ducts being the last to go.

The epithelium is passive throughout and often shows signs of degenerative (especially fatty) change. Sometimes the tissue is inflamed and infiltrated, but this has nothing to do with the emphysema as such: it is simply a concomitant of the catarrh which so frequently affects patients suffering from emphysema.

Chronic emphysema may be due, like the acute variety, to persistent inspiratory over-distention of the lung-tissue. This occurs chiefly in cases where parts of the lung are collapsed and functionless (Art. 592), and the neighboring parts (Fig. 221 *g*) are accordingly over-distended. We might describe this as vicarious or compensatory emphysema. It is

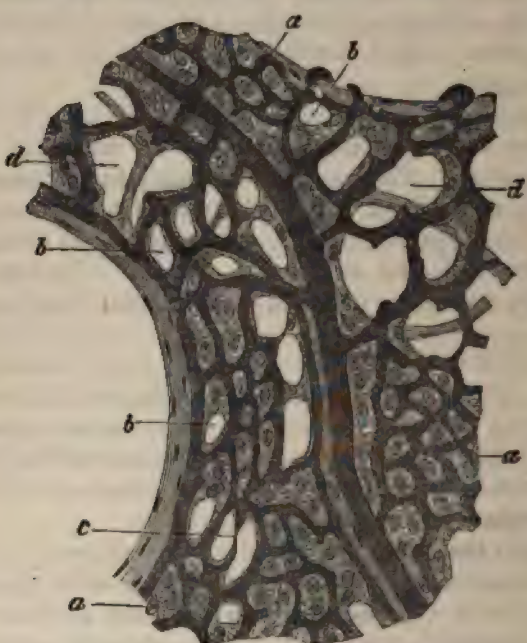


FIG. 222. CHRONIC VESICULAR EMPHYSEMA.

(*Injected preparation, stained with carmine and mounted in Canada balsam* : × 200.)

a, dilated intercapillary spaces with epithelial cells
b, gaps in the alveolar septa (EPPINGER's primary dehiscence)
c, capillary in process of obliteration
d, larger gaps in the alveolar septa and in the capillary network (EPPINGER's secondary dehiscence)

sometimes lobular, sometimes lobar in its extension. The emphysematous lobules are inflated and the alveoli abnormally large.

On the other hand emphysema also results from persistent and violent expiratory efforts, in conditions which interfere with the egress of air from the alveoli, ingress being unimpeded. This is the case in the important variety described as chronic idiopathic diffuse emphysema or simply **general emphysema**, an affection which is very common in persons subject to chronic bronchial catarrh or to frequently-recurring

expiratory dyspnœa, or obliged to make violent expiratory efforts in connection with their employment.

This form of emphysema extends over the whole lung, though it is usually most marked at the edges and apices of the lobes, and at the base. When the lung is removed from the thorax it appears abnormally large, its edges obtuse and rounded, and the base frequently studded with hemispherical bladder-like prominences. The air-vesicles are everywhere enlarged by the disappearance of interalveolar septa, sometimes so much so that they look like bullæ and range in size from that of a pea to that of a hen's egg. The latter is chiefly the case at the

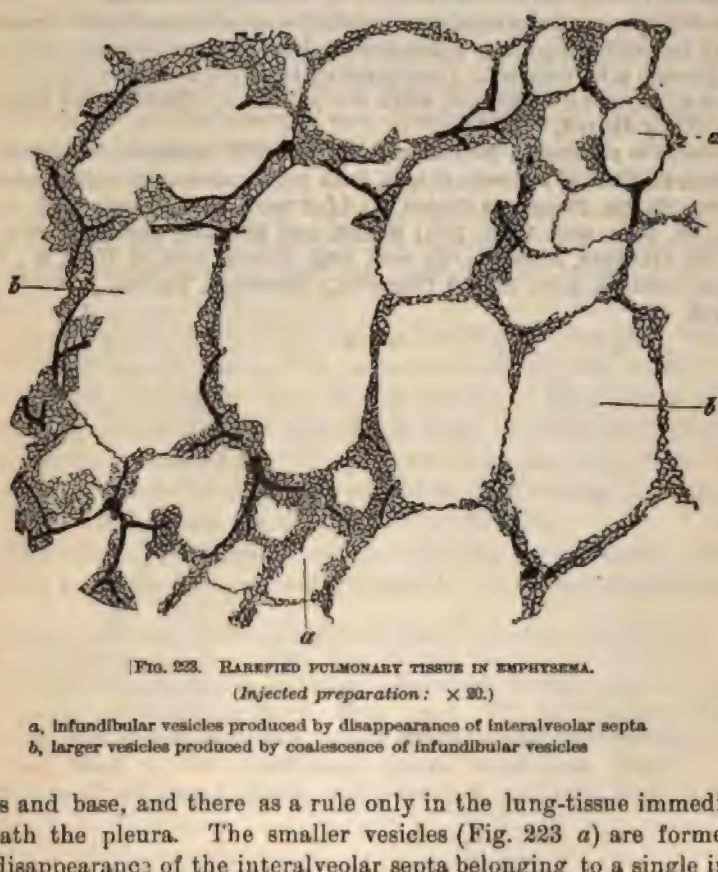


FIG. 223. RAREFIED PULMONARY TISSUE IN EMPHYSEMA.
(*Injected preparation*: × 20.)

a, infundibular vesicles produced by disappearance of interalveolar septa
b, larger vesicles produced by coalescence of infundibular vesicles

edges and base, and there as a rule only in the lung-tissue immediately beneath the pleura. The smaller vesicles (Fig. 223 *a*) are formed by the disappearance of the interalveolar septa belonging to a single infundibulum; the larger vesicles (*b*) to the disappearance of the partitions between adjacent infundibula.

When there is much atrophy of the parenchyma the distended lung feels remarkably soft and downy, and its edges are markedly translucent. If the air is pressed out the lung becomes a mere flaccid inelastic mass with membranous edges.

Chronic idiopathic emphysema is occasionally limited to a part of the lung, usually to the edges. In this case the expiratory obstruction has obviously been also local.

When some of the vesicles in the general or in the local form are of exceptional size we have what is called **bullous emphysema.** The air is usually not easily pressed out of the larger vesicles.

The above account refers the production of emphysema chiefly to mechanical causes, namely to abnormal distention of the alveolar walls; but the atrophy of the latter may be much accelerated by malnutrition or senile decay of the pulmonary tissue. In senile emphysema the latter factor is of essential importance, though the mechanical factors must not be entirely overlooked.

In emphysema a large number of capillaries are obliterated, and the vascular area of the pulmonary artery being thus contracted the resistance to the circulation through it is increased. Compensatory hypertrophy of the right ventricle is thus a frequent concomitant, while the pulmonary arterioles that remain are often visibly dilated.

References :—JENNER, *Med. chir. Trans.* XI. 1857; BIERMER, *Sammlung klin. Vorträge* 12, *Virchow's Handb. d. spec. Path.* V.; KNAUTHE, *Schmidt's Jahrbücher* vol. 163; HERTZ, *Ziemssen's Cyclop.* V.; LICHTHEIM, *Arch. f. exp. Path.* X. 1878; EHEBALD, *Deut. med. Woch.* 1881; RIEGEL and EDINGER, *Zeitschr. f. klin. Med.* 1882–83; VILLEMIN, *Arch. gén. de. méd.* 1866; BAYER, *Arch. d. Heilk.* II.; THIERFELDER, *Atlas d. path. Hist.* I. (Plate VI.); EPPINGER, *Viertelj. f. prakt. Heilk.* vol. 132.

CHAPTER LXXXIV.

DEGENERATIONS OF THE LUNG.

595. The **non-inflammatory degenerations** of the pulmonary tissue are of comparatively slight importance, and have no practical interest for the physician. Emphysema and senile atrophy may form nominal exceptions, and they have already been discussed in Art. 594.

Swelling, fatty degeneration, and desquamation of the pulmonary epithelium accompany every copious transudation into the alveoli, inflammatory or non-inflammatory. The inhalation of deleterious substances also leads to manifold injury of epithelium, blood-vessels, and fibrous stroma; but the changes so induced are of altogether secondary importance in comparison with the inflammation which is at once set up.

Among degenerative changes due to disorders of nutrition we may mention fatty degeneration of the epithelium and amyloid degeneration of the fibrous structures. The former occurs in emphysema and in poisoning by phosphorus and arsenic, the latter in conditions which lead to the like change elsewhere. It is however to be kept in mind that the lung is on the whole but rarely the seat of amyloid change, and that the walls of the blood-vessels are most apt to be affected.

Calcification of the fibrous stroma of the lung is rare, except in cases where the tissue has been morbidly altered by antecedent inflammation.

References :—BUHL, *Lungenentzündung, Tuberculose u. Schwindsucht* 1872 (fatty and amyloid change); CORNIL and BRAULT, *Journ. de. l'anat. et de la physiol.* XVIII. 1882 (phosphorus and arsenic poisoning); CORNIL, *Arch. de physiol.* 1874 (hyaline degeneration); ZAHN, *Virch. Arch.* vol. 72 (stratified corpora amylacea); VON RECKLINGHAUSEN, *Allgem. Path.* Berlin 1883 (ditto); CHIARI, *Wien. med. Woch.* 1, 1878 (calcification); HLAVA, *Wien. med. Blätter* 36, 1882 (calcification of pulmonary vessels); ORTH, *Lehrb. d. spec. path. Anat.* II. Berlin 1885.

CHAPTER LXXXV.

PULMONARY INFLAMMATIONS IN GENERAL.

596. All **acute inflammations** of the lung of any intensity are marked by exudation into the respiratory air-spaces, the exudation following upon an initial congestive hyperæmia of the lung-tissue.

The exudation either consists of a clear albuminous liquid (as in inflammatory œdema), or contains a large number of leucocytes (as in catharrhal or purulent inflammation) or of red blood-cells (hæmorrhagic exudation).

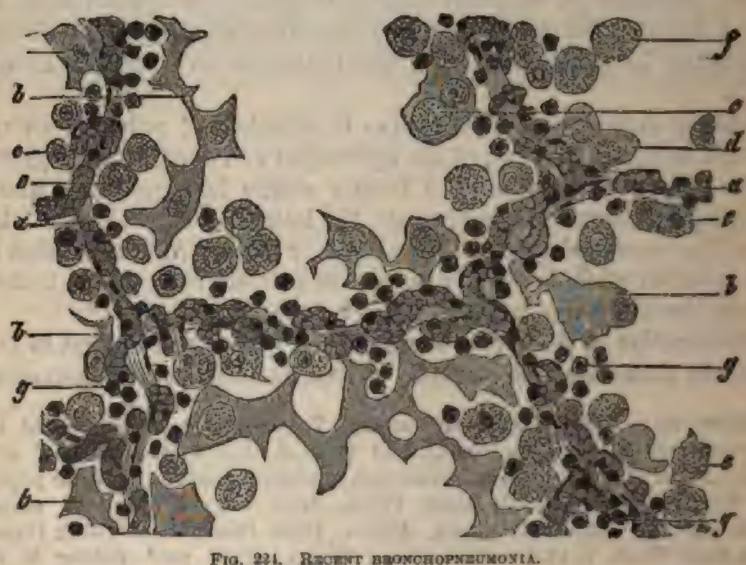


FIG. 224. RECENT BRONCHOPNEUMONIA.

(Section treated with Müller's fluid and picrocarmine, and mounted in glycerine: × 300.)

a, alveolar septa with distended capillaries
b, detached epithelial plates, nucleated and non-nucleated
c d, epithelial plates containing granules and oil-globules around the nuclei
e, detached epithelial cells, nucleus little altered
f, swollen epithelial cells, nucleus obscured by granules
g, leucocytes

This exudation is always followed by more or less marked desquamation of the epithelium lining the alveoli, alveolar ducts, and respiratory bronchioles.

The large nucleated and non-nucleated epithelial plates (Fig. 224 *b*)

are often detached unaltered; when the exudation is sudden and abundant they are often shed in coherent flakes. Oil-globules frequently occur in them (*c*), usually aggregated around the nucleus (*d*).

The small protoplasmic nucleated epithelial cells are also partially detached; many however remain all but unaltered (*e*), appearing only a little swollen or studded with fat-granules (*f*) which to some extent obscure the nucleus.

The blood-vessels are at first distended with blood (*a*), the alveolar septa and walls of the bronchi being saturated with liquid and beset with a moderate number of extravasated leucocytes. The lymphatics also contain some exuded liquid, and the lymphatic glands are swollen. When the onset of the inflammation is less sudden the exudation is at first more scanty, and the epithelial desquamation is accordingly less extensive.

The lung-tissue when recently inflamed is reddened, contains little air or none, and on pressure yields a more or less turbid gray or grayish-red or even blood-stained liquid.

The changes in the pulmonary epithelium and blood-vessels which accompany the beginning of inflammation have frequently been the subject of investigation histological and experimental. Experimenters have set up inflammation in the lung either by cutting the vagus nerve or the recurrent laryngeal nerve, or by injecting irritating liquids such as solution of perchloride of iron or solution (1 per cent) of nitrate of silver. Section of these nerves causes paralysis of the laryngeal muscles, and saliva and other matters get into the air-passages from the mouth. When these are aspirated into the alveoli they set up a local inflammation, which is well-adapted for purposes of investigation.

References:—TRAUBE, *Gesamm. Abhandl.* I. Berlin 1871; COLBERG, *Deut. Arch. f. klin. Med.* II. 1866; FRIEDLÄNDER, *Untersuch. über Lungenentzündung* Berlin 1873, *Virch. Arch.* vol. 68; FREY, *Die path. Lungenveränderungen nach Lähmung d. N. vagi* Leipzig 1877; SOMMERBRODT, *Virch. Arch.* vol. 55; VERAGUTH, *ibid.* vol. 82; WAGNER, *Arch. d. Heilk.* VII., VIII.; CURSCHMANN, *Deut. Arch. f. klin. Med.* XXXII.; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1884; FELD, *Experiment. Beiträge z. Schluck- und Vaguspneumonie* In. Diss. Bonn 1875; FEUERSTACK, *Ueber d. Verhalten d. Epithels d. Lungenalveolen bei d. fibrinösen Pneumonie* Göttingen 1882; HAMILTON, *Pathology of bronchitis* London 1883.

597. When the exudation has reached its highest point the affected tissue is usually devoid of air, the alveoli being filled with the exuded matters and with desquamated epithelium. We may distinguish certain varieties of pulmonary inflammation by the nature of the accompanying exudation.

In **hæmorrahagic inflammation** the chief contents of the alveoli are red blood-corpuscles, and the inflamed region has a dark-red or brown color.

In **catarrhal inflammation** the contents of the alveoli consist mainly of liquid and small rounded cells with some admixture of larger

squamous cells (Fig. 225). When these larger cells are the more numerous (Fig. 225 c) the affection is often spoken of as desquamative catarrh, the assumption being that the large cells are detached alveolar epithelial plates. This is however by no means always the case, for such cells are not infrequently developed from extravasated leucocytes. A portion of lung affected with catarrh looks red, grayish-red, gray, or grayish-yellow according as it contains much or little blood; on pressure it yields a grayish liquid more or less mingled with blood.

Croupous inflammation is characterized by the coagulation of the exudation, fine threads of fibrin appearing between the cells contained in the extravasated liquid (Fig. 226) and making the whole cohere into a compact semi-solid mass.

Coagulated exudations of this kind consist chiefly of liquid mingled with red and white blood-cells and epithelium, coagulation setting in as the white blood-cells dissolve.

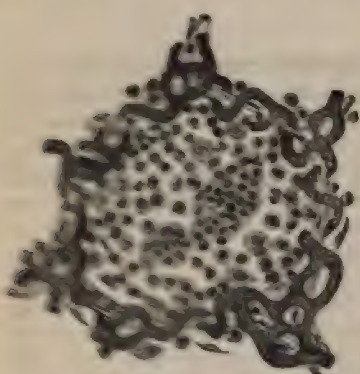


Fig. 225.

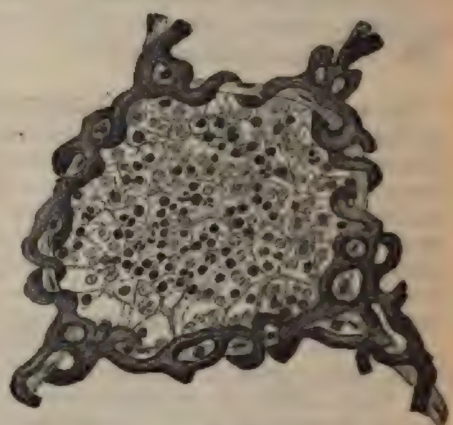


Fig. 226.

Fig. 225. Catarrhal bronchopneumonia.

(Injected preparation stained with hæmatoxylin: × 80.)

An alveolus filled with liquid and with large and small colorless cells

Fig. 226. Croupous pneumonia (red hepatization).

(Injected preparation stained with hæmatoxylin: × 80.)

An alveolus filled with a coagulated exudation containing red and white corpuscles and epithelial cells

Another form of coagulation is observed in exudations containing many large cells (Fig. 227) and tending to become caseous at a later stage. In these the cells break up and dissolve entirely, forming with the exuded liquid a granular and fibrinous mass (*d*): when recent this contains a few nuclei, but soon these too disappear and the mass becomes uniformly fibrinous. The two forms of coagulation are met with in combination.

The coagulated exudation is more or less solid, and the affected

parenchyma accordingly becomes firm and resistant, resembling liver in consistence: the condition is therefore described as **hepatization** of the lung. The surface on section is usually rough and granulated, the coagula projecting somewhat from the cut alveolar walls. The color varies from deep-red (red hepatization) to grayish-red or grayish-yellow (gray hepatization), according to the amount of blood that is present and the composition of the exudation.

In many forms of pulmonary inflammation the changes within the contents of the alveoli are those that are most striking and important, the changes in the parenchyma itself being of secondary significance. These forms have been described as superficial in contradistinction to interstitial inflammations; in the latter marked changes (infiltration, hyperplasia, etc.) are simultaneously set up in the connective tissues

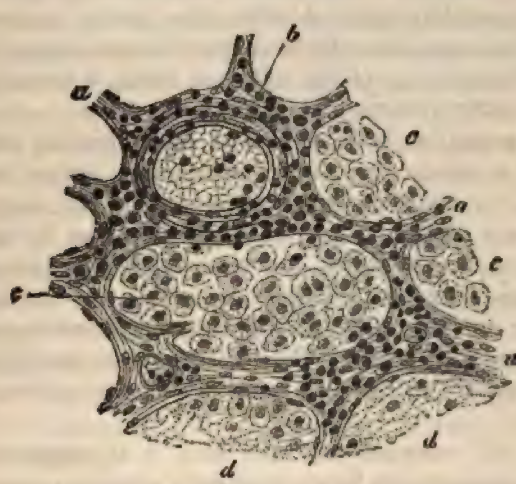


FIG. 227. CASEATING LOBULAR BRONCHOPNEUMONIA.

(*Section hardened in alcohol and stained with hæmatoxylin* : × 120.)

a, alveolar septa infiltrated with cells
b, venule with infiltrated wall
c, alveoli filled with large epithelioid cells
d, alveolar contents consisting of granular and fibrinous coagula

(Fig. 227 *a b*). The distinction can frequently be made, but it is not exactly one of kind, as the two forms pass the one into the other through a number of transitional stages.

Cellular infiltration of the lung-tissue is never entirely absent in any pulmonary inflammation; but in some varieties it is slight and transient, in others intense and persisting. There is always in like manner a certain amount of exudation into the lymphatic vessels.

The extent of the inflammatory change varies greatly in different cases, and accordingly we have forms described as miliary, nodular, lobular, and lobar.

When the inflamed part of the lung is close to the pleural surface, the pleura in general becomes inflamed at the same time. Hyperæmia is first induced, and a more or less abundant exudation is then poured out on the free surface.

598. **Terminations of pulmonary inflammation.** The most favorable issue is in **resolution**, the exudation being removed and the altered tissue restored. The exudation may be removed by expectoration, but the greater part is re-absorbed.

In many forms of inflammation the pulmonary vessels continue permeable to injections throughout the entire course of the affection (Figs. 225, 226), and the lymphatics in like manner are not permanently obstructed by the inflammatory exudation. Resorption therefore goes on continuously, the exuded matters being carried off directly in a more or less altered condition. Coagulated and cellular exudations must of course become partially liquefied before they can be re-absorbed. This liquefaction is brought about by fatty and mucoid change and by disintegration and breaking up of the cells and fibrin, a turbid pulpy liquid containing granular detritus is thus formed.

While the exudation is in process of disintegration within the pulmonary tissue a certain amount of inflammatory action persists, manifested chiefly by the continued extravasation of leucocytes. The leucocytes play a part in the process of resorption by taking up into their protoplasm fragments of the unliquefied detritus and carrying these with them into the lymphatic channels. At the same time the loss of alveolar epithelium is made good by regenerative multiplication of the intact epithelial cells. When the new cells continue to be shed as they are produced we have the condition known as chronic desquamative catarrh.

A second but comparatively rare issue is in **suppuration.** It is characterized anatomically by an extremely abundant accumulation of leucocytes within the alveoli and in their walls, together with progressive disintegration and liquefaction of the latter. This destructive process is set up by the presence of some intensely irritant agent, giving rise to ferments which dissolve the pulmonary tissue.

A third issue, also not very common, is in **gangrene.** The conditions for its appearance are—first, extreme disturbance and in parts suppression of the circulation, and secondly, the presence in the affected part of putrefactive micro-organisms. The gangrenous tissue is transformed into a dark-brown dirty mass, changing presently into a greenish-black foul-smelling sanious pulp or pus: this at first contains shreds and fragments of pulmonary tissue, but these too at length dissolve and disappear. The gangrenous pus contains various chemical products of disintegration of albumen and fat, such as leucin, tyrosin, margarin, volatile fatty acids, especially butyric, sulphuretted hydrogen, ammonia, etc. The more solid contents include granular detritus, pus-corpuscles,

pigment, shreds of lung-tissue, oil-globules, margarin-needles, crystals of triple-phosphate, and various micro-organisms. The latter are the prime cause of the chemical decomposition and of the disintegration of the pulmonary tissue. According to FILEHNE a certain ferment is formed by them which acts like trypsin, and in alkaline solutions quickly dissolves elastic tissue.

Caseation most frequently occurs as a sequel of tuberculous inflammation, though it is also not entirely absent in the other forms. It would thus appear to depend upon some peculiar property of the exciting cause of the inflammation, though under special conditions it may occur in connection with inflammations which usually terminate in a more favorable way. So far as mere morbid anatomy is concerned we may say that caseation takes place most frequently in inflammations which are characterized by dense cellular infiltration of the parenchyma of the lung and accompanied by extensive alteration of the walls of the lymphatics and blood-vessels. The latter feature is most marked in tuberculous inflammation, and thus the anatomical and the ætiological characters are in this regard largely co-extensive.

In caseous degeneration the exudation within the aveoli necroses, and is in the first instance transformed into a fibrinous and granular mass (Fig. 227). In other cases it appears homogeneous, or the extravasated cells lose their nuclei and break down into fatty granular detritus. As a rule the alveolar walls also become speedily necrotic and caseous. The vessels are blocked up, the nuclei of the tissue-cells disappear, the contours of the tissue-fibres become indistinct, and at length the pulmonary tissue becomes granular or homogeneous and structureless, almost or altogether indistinguishable from the caseous exudation proper. When the walls of the larger vessels have been much infiltrated they too become caseous in like manner.

The last and not uncommon termination of a pulmonary inflammation is in the formation of new fibrous tissue and **cirrhosis.**

New fibrous tissue is developed when the cellular infiltration of the parenchyma of the lung is long-continued, the circulation at the same time remaining ample for the nutrition of the part. In such conditions large formative or fibroblastic cells make their appearance first in the alveolar walls (Fig. 228 *a*) and in the circumvascular, peribronchial, and interlobular connective tissue, and at length in the pleura also. These cells develop into fibrous tissue in the usual way (Art. 108), and so give rise to thickening of the affected parts and consequently to diminution of the respiratory spaces. As collapse very commonly accompanies this fibroid change the thickened alveolar walls speedily come into contact and cohere, and the corresponding aveolar cavities are obliterated. Some of the alveoli however may remain open, and these become lined with short cylindrical epithelial cells, so that on section they somewhat resemble the acini of a gland.

Not infrequently the fibrous hyperplasia in the alveolar walls is accompanied by a like development within the alveoli: large epithelioid formative cells (Fig. 228 *d*) make their appearance in the alveolar contents, and growing out as bands or strings of cells (*e*) or as bud-like processes from the alveolar wall traverse the exudation in various directions. At the same time buds and outgrowths spring from the capillaries of the alveolar wall (*g*); these push their way into the new tissue and being transformed into blood-vessels provide for its nutrition. The whole process corresponds closely with that by which a thrombus is organized (Art. 255).

Pulmonary tissue thus thickened by fibroid induration is firm and tough and usually devoid of air. Its color varies from white to slaty-gray or even black, according to the amount of pigment present.

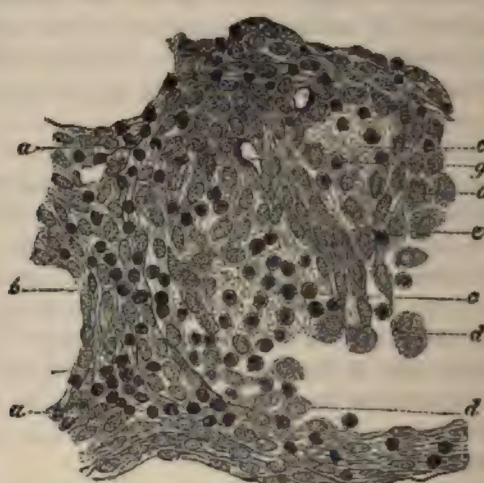


FIG. 228. GROWTH OF FIBROUS TISSUE IN THE WALLS AND IN THE CONTENTS OF AN ALVEOLUS.

(*Hæmatoxylin staining:* × 150.)

a, alveolar wall thickened and fibroid
b, small leucocytes
c, fibrinous and cellular exudation
d, intra-alveolar formative cells
e, string of fusiform fibroblasts
g, new-formed blood-vessels

Caseation and fibroid induration are very frequently met with in combination, the caseous foci being surrounded and enclosed by new and cellular fibrous tissue.

599. **Causes of pulmonary inflammation.** The inflammations of the lung are set up by irritants reaching it by way of the blood-vessels or of the bronchi, or by extension from the pleura or mediastinum. We may therefore conveniently consider these inflammations according to their various modes of origin.

As regards the pulmonary inflammations whose exciting cause is referable to the blood it must be observed that the lung is not on the whole so liable as other organs to be the seat of contaminating deposit

from the blood. Thus pigment-granules and micro-organisms may circulate freely through the capillaries of the lung without being arrested; this is doubtless due to the fact that the capillaries are comparatively wide and the blood-stream rapid. Deposits from the blood do however occur, and thus we meet with forms of hæmatogenous infiltration and hæmatogenous (bacterial) infection.

When the blood contains an excessive proportion of white corpuscles, these may accumulate in great numbers in the capillaries of the lung, and by extravasation in the tissues also, and give rise to **leukæmic infiltration.** Fat and oil-globules circulating in the blood (as in lipæmia) are apt to collect in the pulmonary vessels causing fatty embolism; and in anthrax the specific bacilli frequently crowd the capillaries so as to look like an artificial injection of them.

Four kinds of hæmatogenous infective inflammation are described; they may be described as **pneumonias** in a restricted sense of the term. They are—true croupous pneumonia, embolic septic (suppurative or gangrenous) pneumonia, embolic tuberculosis, and embolic syphilis. They are probably all due to bacterial infection, and we must assume that the bacteria are conveyed by the blood.

What we may term the **pleurogenous pneumonias** are closely allied to those just referred to. The inflammatory process extends from the pleura to the lung-tissue chiefly along the interlobular lymphatic channels, though here and there it passes thence directly to the peribronchial tissue and to the pulmonary parenchyma. The antecedent pleuritic affection is generally itself hæmatogenous. Traumatic pneumonia may be considered as a special pleurogenous variety, pleura and lung being generally injured simultaneously.

An inflammation of the lung induced by an irritant conveyed to the parenchyma by the bronchi is described as a **broncho-pneumonia.** It is immaterial whether the bronchi themselves are previously or simultaneously inflamed or not.

600. **Inhaled impurities.** The lungs are by reason of their function exposed to the access of numerous impurities. We all inhale a certain amount of dust with the air of the street or of the house, while in certain occupations the amount of dust necessarily inhaled is very considerable. Workers in stone of all kinds, masons, bricklayers, potters, inhale mineral and earthy dust; workers in metal such as grinders, gilders, braziers, typefounders, and so on, inhale metallic particles; millers, colliers, coal-heavers, chimney-sweeps, bakers, cabinet-makers, rope-makers, cigar-makers, and workers in spinning and weaving mills, live in an atmosphere charged with dust of vegetable origin. Brushmakers, upholsterers, barbers, cloth-dressers, and hat-makers breathe air containing animal dust; and glass-workers, street-sweepers, etc. dust of various other kinds.

A large proportion of the dust thus inhaled is caught in the air-

squamous cells (Fig. 225). When these larger cells are the more numerous (Fig. 227 *c*) the affection is often spoken of as desquamative catarrh, the assumption being that the large cells are detached alveolar epithelial plates. This is however by no means always the case, for such cells are not infrequently developed from extravasated leucocytes. A portion of lung affected with catarrh looks red, grayish-red, gray, or grayish-yellow according as it contains much or little blood; on pressure it yields a grayish liquid more or less mingled with blood.

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Coagulated exudations of this kind consist chiefly of liquid mingled with red and white blood-cells and epithelium, coagulation setting in as the white blood-cells dissolve.

FIG. 225.

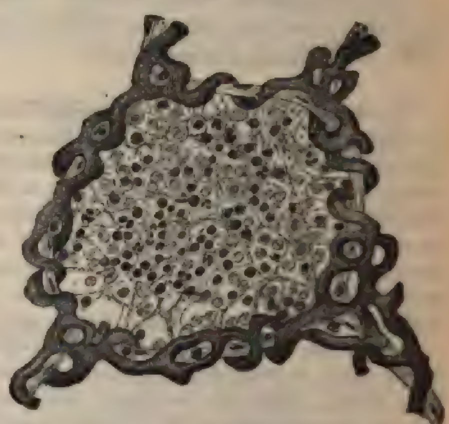

FIG. 226.

FIG. 225. CATARRHAL BRONCHOPNEUMONIA.

(*Injected preparation stained with hæmatoxylin :* × 80.)

An alveolus filled with liquid and with large and small colorless cells

FIG. 226. CROUPOUS PNEUMONIA (RED HEPATIZATION).

(*Injected preparation stained with hæmatoxylin :* × 80.)

An alveolus filled with a coagulated exudation containing red and white corpuscles and epithelial cells

Another form of coagulation is observed in exudations containing many large cells (Fig. 227) and tending to become caseous at a later stage. In these the cells break up and dissolve entirely, forming with the exuded liquid a granular and fibrinous mass (*d*): when recent this contains a few nuclei, but soon these too disappear and the mass becomes uniformly fibrinous. The two forms of coagulation are met with in combination.

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parenchyma accordingly becomes firm and resistant, resembling liver in consistence: the condition is therefore described as **hepatization** of the lung. The surface on section is usually rough and granulated, the coagula projecting somewhat from the cut alveolar walls. The color varies from deep-red (red hepatization) to grayish-red or grayish-yellow (gray hepatization), according to the amount of blood that is present and the composition of the exudation.

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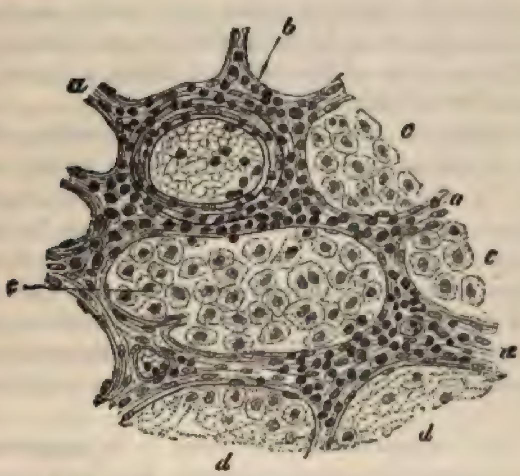

FIG. 227. CASEATING LOBULAR BRONCHOPNEUMONIA.

(Section hardened in alcohol and stained with hæmatoxylin : × 120.)

a, alveolar septa infiltrated with cells
b, venule with infiltrated wall
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d, alveolar contents consisting of granular and fibrinous coagula

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Cellular infiltration of the lung-tissue is never entirely absent in any pulmonary inflammation; but in some varieties it is slight and transient, in others intense and persisting. There is always in like manner a certain amount of exudation into the lymphatic vessels.

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pigment, shreds of lung-tissue, oil-globules, margarin-needles, crystals of triple-phosphate, and various micro-organisms. The latter are the prime cause of the chemical decomposition and of the disintegration of the pulmonary tissue. According to FILEHNE a certain ferment is formed by them which acts like trypsin, and in alkaline solutions quickly dissolves elastic tissue.

Caseation most frequently occurs as a sequel of tuberculous inflammation, though it is also not entirely absent in the other forms. It would thus appear to depend upon some peculiar property of the exciting cause of the inflammation, though under special conditions it may occur in connection with inflammations which usually terminate in a more favorable way. So far as mere morbid anatomy is concerned we may say that caseation takes place most frequently in inflammations which are characterized by dense cellular infiltration of the parenchyma of the lung and accompanied by extensive alteration of the walls of the lymphatics and blood-vessels. The latter feature is most marked in tuberculous inflammation, and thus the anatomical and the ætiological characters are in this regard largely co-extensive.

In caseous degeneration the exudation within the aveoli necroses, and is in the first instance transformed into a fibrinous and granular mass (Fig. 227). In other cases it appears homogeneous, or the extravasated cells lose their nuclei and break down into fatty granular detritus. As a rule the alveolar walls also become speedily necrotic and caseous. The vessels are blocked up, the nuclei of the tissue-cells disappear, the contours of the tissue-fibres become indistinct, and at length the pulmonary tissue becomes granular or homogeneous and structureless, almost or altogether indistinguishable from the caseous exudation proper. When the walls of the larger vessels have been much infiltrated they too become caseous in like manner.

The last and not uncommon termination of a pulmonary inflammation is in the formation of new fibrous tissue and **cirrhosis.**

New fibrous tissue is developed when the cellular infiltration of the parenchyma of the lung is long-continued, the circulation at the same time remaining ample for the nutrition of the part. In such conditions large formative or fibroblastic cells make their appearance first in the alveolar walls (Fig. 228 *a*) and in the circumvascular, peribronchial, and interlobular connective tissue, and at length in the pleura also. These cells develop into fibrous tissue in the usual way (Art. 108), and so give rise to thickening of the affected parts and consequently to diminution of the respiratory spaces. As collapse very commonly accompanies this fibroid change the thickened alveolar walls speedily come into contact and cohere, and the corresponding aveolar cavities are obliterated. Some of the alveoli however may remain open, and these become lined with short cylindrical epithelial cells, so that on section they somewhat resemble the acini of a gland.

Not infrequently the fibrous hyperplasia in the alveolar walls is accompanied by a like development within the alveoli: large epithelioid formative cells (Fig. 228 *d*) make their appearance in the alveolar contents, and growing out as bands or strings of cells (*e*) or as bud-like processes from the alveolar wall traverse the exudation in various directions. At the same time buds and outgrowths spring from the capillaries of the alveolar wall (*g*); these push their way into the new tissue and being transformed into blood-vessels provide for its nutrition. The whole process corresponds closely with that by which a thrombus is organized (Art. 255).

Pulmonary tissue thus thickened by fibroid induration is firm and tough and usually devoid of air. Its color varies from white to slaty-gray or even black, according to the amount of pigment present.

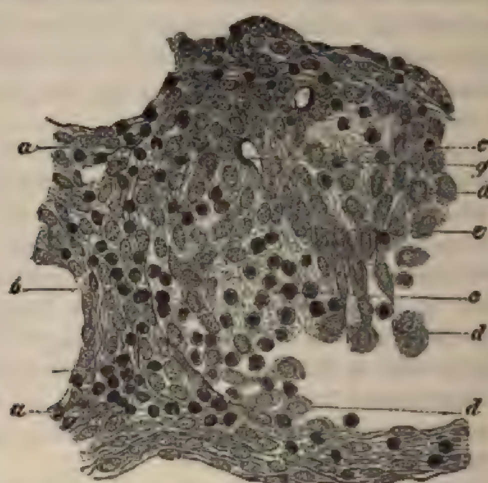

FIG. 228. GROWTH OF FIBROUS TISSUE IN THE WALLS AND IN THE CONTENTS OF AN ALVEOLUS.

(*Hæmatoxylin staining:* × 150.)

a, alveolar wall thickened and fibroid
b, small leucocytes
c, fibrinous and cellular exudation
d, intra-alveolar formative cells
e, string of fusiform fibroblasts
g, new-formed blood-vessels

Caseation and fibroid induration are very frequently met with in combination, the caseous foci being surrounded and enclosed by new and cellular fibrous tissue.

599. **Causes of pulmonary inflammation.** The inflammations of the lung are set up by irritants reaching it by way of the blood-vessels or of the bronchi, or by extension from the pleura or mediastinum. We may therefore conveniently consider these inflammations according to their various modes of origin.

As regards the pulmonary inflammations whose exciting cause is referable to the blood it must be observed that the lung is not on the whole so liable as other organs to be the seat of contaminating deposit

from the blood. Thus pigment-granules and micro-organisms may circulate freely through the capillaries of the lung without being arrested; this is doubtless due to the fact that the capillaries are comparatively wide and the blood-stream rapid. Deposits from the blood do however occur, and thus we meet with forms of hæmatogenous infiltration and hæmatogenous (bacterial) infection.

When the blood contains an excessive proportion of white corpuscles, these may accumulate in great numbers in the capillaries of the lung, and by extravasation in the tissues also, and give rise to **leukæmic infiltration.** Fat and oil-globules circulating in the blood (as in lipæmia) are apt to collect in the pulmonary vessels causing fatty embolism; and in anthrax the specific bacilli frequently crowd the capillaries so as to look like an artificial injection of them.

Four kinds of hæmatogenous infective inflammation are described; they may be described as **pneumonias** in a restricted sense of the term. They are—true croupous pneumonia, embolic septic (suppurative or gangrenous) pneumonia, embolic tuberculosis, and embolic syphilis. They are probably all due to bacterial infection, and we must assume that the bacteria are conveyed by the blood.

What we may term the **pleurogenous pneumonias** are closely allied to those just referred to. The inflammatory process extends from the pleura to the lung-tissue chiefly along the interlobular lymphatic channels, though here and there it passes thence directly to the peribronchial tissue and to the pulmonary parenchyma. The antecedent pleuritic affection is generally itself hæmatogenous. Traumatic pneumonia may be considered as a special pleurogenous variety, pleura and lung being generally injured simultaneously.

An inflammation of the lung induced by an irritant conveyed to the parenchyma by the bronchi is described as a **broncho-pneumonia.** It is immaterial whether the bronchi themselves are previously or simultaneously inflamed or not.

600. **Inhaled impurities.** The lungs are by reason of their function exposed to the access of numerous impurities. We all inhale a certain amount of dust with the air of the street or of the house, while in certain occupations the amount of dust necessarily inhaled is very considerable. Workers in stone of all kinds, masons, bricklayers, potters, inhale mineral and earthy dust; workers in metal such as grinders, gilders, braziers, typefounders, and so on, inhale metallic particles; millers, colliers, coal-heavers, chimney-sweeps, bakers, cabinet-makers, rope-makers, cigar-makers, and workers in spinning and weaving mills, live in an atmosphere charged with dust of vegetable origin. Brush-makers, upholsterers, barbers, cloth-dressers, and hat-makers breathe air containing animal dust; and glass-workers, street-sweepers, etc. dust of various other kinds.

A large proportion of the dust thus inhaled is caught in the air-

passages, but some of it especially in deep inspiration is carried into the parenchyma of the lung. Many of the particles adhere to the walls of the alveoli; others are promptly conveyed into the lymphatic channels communicating with the alveoli, and thence are carried by the peribronchial and interlobular lymphatics into the lymphatic glands at the root of the lung.

When a considerable number of dust-particles reach the parenchyma of the lung they set up a slight inflammation manifested by emigration of white blood-cells from the vessels and the desquamation of some of the alveolar epithelial cells.

The extravasated cells take up the foreign particles, sometimes in such abundance that they have been fitly termed **dust-cells** (LANGHANS, VON INS). They may be carried into the bronchioles and bronchi and are then ejected with the sputa. Much the larger number of them are however carried into the lymphatics.

Within the lymphatics certain kinds of dust, such as chalk-particles, are dissolved. Insoluble dusts are either carried into the bronchial glands or are deposited in the walls of the lymphatic vessels. This deposit takes place wherever lymphatics occur, that is in the interalveolar, interlobular, subpleural, pleural, circumvascular, and peribronchial fibrous tissues, especially in those parts where aggregations of lymphoid elements are normally met with. The particles lie either free in the tissues or enclosed in rounded, fusiform, or stellate cells.

Colored dust gives rise to pigmentation of the lung, while the larger grains appear as sandy or gritty deposits. Some forms of dust-deposit, in particular those which give rise to marked change in the lung, have received special names. The most frequent as well as the best-known form is that due to the inhalation of soot or coal-dust, by which the lung becomes dark-gray or black; it is variously described as **anthracosis** or *pneumonoconiosis anthracotica* (κονις dust, ανθραξ coal), and the lung as collier's or **miner's lung.** This form of pigmentation is very common, and is seldom entirely absent in adult lungs. It must however be remembered that all black pigmentations of the lung are not anthracotic, for black pigment is frequently a derivative of the coloring-matter of the blood (Arts. 68, 268). A second form is the so-called **siderosis** (compare Art. 268) or *pneumonoconiosis siderotica* (σιδηρος iron) of ZENKER, due to the inhalation of metallic dust; in the lung it appears as oxide or sesquioxide or phosphate of iron. Oxide of iron (rouge) is used as a pigment and as a polishing-material; it gives rise to a brick-red pigmentation of the lung, the other iron-compounds tending rather to blacken it. The deposit of stone-dust, especially of quartz, flint, and glass, has been called **chalicosis** (χαλιξ grit); dust from clay as inhaled by porcelain-workers and makers of artificial ultramarine gives rise to **aluminosis.** Grinders inhale mixtures of steel-dust and

grit which cause the affection known as **grinder's asthma** or grinder's rot.

PEARSON, THOMSON, ROBIN and others surmised that part at least of the black pigmentation so frequently found in the lung was derived from inhaled soot and coal-dust: TRAUBE verified this by actually demonstrating the presence of microscopic particles of coal in the lung and sputum. COHNHEIM thinks that the black pigment of the lung is entirely of this nature; but VIRCHOW is no doubt right in referring some of it to altered blood-pigment. ZIEGLER has found that in a very large number of cases the lung-tissue and the bronchial glands contain broken-down red corpuscles, corpuscle-carrying cells, yellow and brown flakes, and granules of pigment. This is especially the case in parts that have been altered in any way by inflammation.

ZENKER'S researches were the first to give us precise information on siderosis. KUSSMAUL, SCHMIDT, and MEINEL have examined the mineral residue (ash) of lung-tissue, and have shown that in chalicosis the amount of silica present is remarkably increased. LEWIN, VILLARET, CROCQ, VON INS, RUPPERT, SCHOTTELIUS, and others have experimented on dust-inhalation.

References:—PEARSON, *Phil. Trans.* 1813; THOMSON, *Med. chir. Trans.* XX., XXI. (1837); ROBIN, *Traité de chimie anatomique* III. (1853); TRAUBE, *Deutsche Klinik* 1860; ZENKER, *Deut. Arch. f. klin. Med.* XIII.; KUSSMAUL, *ibid.* II.; GREENHOW, *Lancet* 1, 1869, *Trans. Path. Soc.* XVI. *et seq.*, *Report of Med. Off. to Privy Council* 1861; MEINEL, *Deut. Viertelj. f. öffentl. Gesundh.* 1876; VIRCHOW, *Virch. Arch.* vols. 1, 35, *Edin. Med. Journ.* 1858; LEWIN, *Beiträge z. Inhalationstherapie* Berlin 1863; VILLARET and CROCQ, *Schmidt's Jahrb.* 116, 126; VON INS, *Arch. f. exp. Path.* V.; KNAUFF, *Virch. Arch.* vol. 39; SLAVJANSKY *ibid.* vol. 48; RUPPERT, *ibid.* vol. 72; SOYKA, *Prag. med. Woch.* 1878; MERKEL, *Ziemssen's Cyclop.* I.; HIRT, *Staubinhalationskrankheiten* Breslau 1871; SMITH, *Med. Times* 1, 1881; HESSE, *Viertelj. f. gerichtl. Med.* XXXVI. (1882); SELIGSOHN, *Eulenburg's Realencyclopädie* Article *Staubkrankheiten*; WEICHSELBAUM, *Cent. f. med. Wiss.* 1882, *Wiener med. Jahrb.* 1883; BUHL, *Naturforscherversammlung in München* 1877; HARRIS, *Journ. of Anat. and Physiol.* XV. 1881; ARNOLD, *Staubinhalation* Leipzig, 1885.

601. The kinds of dust described in the last article, when in small quantities, give rise to no serious change in the lung, other than pigmentation. This is especially true of coal-dust of which very considerable quantities may be inhaled without injury. Metal-dust and grit are more dangerous, for in any but small amounts they set up inflammations which in some cases are not slight or transient but give rise to very marked alteration in the lungs. Dust-inhalation is thus the exciting cause of a group of bronchopneumonic affections ending in chronic pulmonary change.

If insoluble dust is capable of acting in this way, much more will dust containing soluble chemically-active substances, and organized or microparasitic irritants.

The air we breathe, especially in thickly-populated places, very frequently contains such matters, and some of them must reach the lung and be deposited on the alveolar walls or enter its tissue or the lymphatics. Many of them do no noticeable harm, others and especially the

micro-organisms pass from the lung into other parts of the body, and act as the specific causes of infective disease. Others again give rise to local inflammatory change in the lung itself at the places where they settle. The bacillus of tuberculosis (or its spores) is probably the most striking example, and there is no doubt that other disease-producing agents reach and act on the lung in a similar way.

In addition to these irritants inhaled with the air from the atmosphere without, we may have disease set up by inhalation of matters derived from the body itself, and carried into the alveoli of the lung from the mouth, nose, pharynx, larynx, or air-tubes. Saliva and particles of food may be aspirated instead of swallowed, and pus from the larynx or bronchi may be carried into the respiratory parenchyma instead of being coughed up. The former occurs in very young or comatose patients, and the latter in those suffering from laryngitis or bronchitis.

These substances when thus aspirated usually set up more or less intense inflammation, especially when they are putrescent or contain putrefactive organisms, or specifically virulent agents such as the bacilli of tuberculosis or of glanders.

Very various forms of bronchopneumonia, specific and non-specific, are thus induced, their course and character depending on the nature of the exciting cause. Tubercle-bacilli give rise to inflammatory processes tending to caseation; the products of catarrhal bronchitis as a rule set up a similar catarrhal bronchopneumonia, slight and usually transient in character; pus from a perichondritic laryngeal abscess tends to cause violent suppurative inflammation of the lung, and putrescent particles of food may lead to gangrene.

Many experiments have been made on the action of saliva, decomposing organic substances, and bacteria, when aspirated into the lung. The numerous experiments on so-called **vagus-pneumonia** are of this nature. This form of inflammation is observed when the vagus and recurrent laryngeal nerve are cut, and is due to the fact that the paralyzed larynx permits saliva and foreign matters from the mouth to be drawn into the lung. Other investigators have conveyed into the bronchi liquids or pulverulent matters (dry or suspended in water), others again have caused animals to breathe various substances suspended in the air by means of spray. LIPPL, TAPPEINER, SCHWENINGER, SCHOTTELIUS, WEICHSELBAUM, VERAGUTH, and others have in this way tested the infectiveness of phthisical sputum.

The result of such inhalation-experiments depends on the nature of the matters inhaled and on the mode of experimentation. When finely-divided irritant substances, such as spray of phthisical sputum or of putrid liquids, are inhaled, small miliary bronchopneumonic foci are produced. When the inhaled matters are coarser or of larger volume, and of an irritant nature, we have large usually lobular patches of inflammation with hæmorrhage, suppuration, or gangrene, as the case may be. When the foreign matters are bulky enough to occlude one or more of the bronchioles the first effect is partial collapse or atelectasis. Large quantities of liquid quickly introduced into the lung may lead, as in drowning, to death by asphyxia. The liquid is carried with the inspired air into the alveoli, and fills them with a mass of froth.

References:—Art. 596; TRAUBE, *Beiträge z. Path. u. Phys.* I. Berlin 1871; BODDAERT *Lésions pulmon. consée. à la section d. nerfs pneumogastriques* Brussels 1862; FRIEDLÄNDER, *Untersuch. üb. Lungenentzündung* Berlin 1873, *Virch. Arch.* vol. 68; FREY, *Die path. Lungenveränderungen nach Lähmung d. Nervi vagi* Leipzig 1877; SCHOTTELIUS, *Virch. Arch.* vol. 73; BUHL, TAPPEINER, LIPPL, SCHWENINGER, *Naturforscherversammlung in München* 1877; TAPPEINER, *Virch. Arch.* vols. 73, 82; HEIDENHAIN, *ibid.* vol. 70 (inhalation of hot steam).

10

CHAPTER LXXXVI.

FORMS OF PNEUMONIA.

602. **Croupous pneumonia** is an inflammation of one or more lobes of the lung, and is the characteristic symptom of a certain specific infective disease. The disease is acute, and the anatomical change which accompanies it is the appearance of a firm or solid exudation within the pulmonary alveoli.

The exudation may be limited to a portion of one lobe or appear in several isolated patches; but more usually it extends over the greater part or the whole of one lobe, or over the entire lung. Occasionally indeed both lungs are affected. The exudation either reaches its full extent suddenly and rapidly, or advances by successive stages.

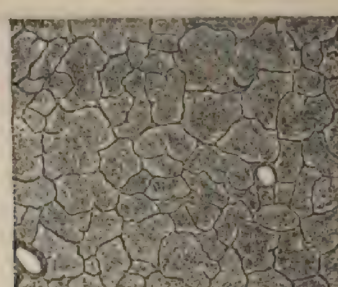

FIG. 229. CROUPOUS HEPATIZATION OF THE LUNG.

(Hardened in Müller's fluid and stained with alum-carmine: × 80.)

The process begins with intense congestive hyperæmia, by reason of which the lung appears of a deep red color. This is the stage of **congestion** (*engouement*). The hyperæmia is accompanied by exudation from the vessels, by which in a short time the air is driven out of the alveoli, alveolar ducts, and respiratory bronchioles. At the same time the protoplasmic epithelial cells, and the homogeneous plates lining these spaces, are at least in part detached or shed (Fig. 224, Art. 596).

The alveolar contents thus consist (Fig. 226, Art. 597) of albuminous liquid, red and white blood-cells, and desquamated pulmonary epithelium. After a time coagulation takes place, granules and filaments appearing between and uniting the cellular elements into a solid mass adhering to the internal surface of the alveolus.

The coagulation of the exudation marks the beginning of the stage of **red hepatization** (Fig. 229). The lung is bulky, heavy, firm, and airless. The cut surface is red or grayish-red and granulated, the plugs which distend the alveoli protruding somewhat beyond their walls. The pleura over the affected region is turbid and covered with a thin film of fibrin: the costal surface is often marked by shallow impressions of the ribs. In the neighborhood of the infiltrated region the lung-tissue is frequently œdematous or filled with a turbid grayish exudation containing numerous leucocytes.

During the stage of red hepatization the lung is still highly vascular and filled with blood, the red tint being due not only to the extravasated red corpuscles but also to the blood which distends the capillaries. When the red corpuscles are extravasated in very large numbers the exudation assumes a dark-red tint like that of hæmorrhagic infiltration.

The stage of red hepatization passes gradually into that of **gray hepatization.** The change of tint is mainly due to the decolorization of the exudation and the accompanying anæmia of the lung-tissue. It must be remembered that in ordinary cases the pulmonary vessels remain throughout permeable by injections, while the normal structure of the lung continues quite distinct (Fig. 229). As the exudation loses color the cells it contains break down by fatty change and disintegration into granules and flakes, and they with the fibrin begin to dissolve. Leucocytes now migrate freely from the vessels, some of which remain clinging to the vessel-walls while others mingle with the liquefying exudation.

These changes result in the **colliquation** of the firm coagula, and when the lung is cut and scraped an abundant turbid whitish or grayish juice comes away, and the plugs that still fill the alveoli are loose and easily removed. The **resolution** of the pneumonia has set in.

The bronchi of the affected part are throughout the changes just described the seat of inflammatory change, and contain a mucous or sero-mucous secretion stained brown or red ('prune-juice' or 'rusty' sputum) with blood pigment. In the later stages the secretion is mingled with liquefied exudation from the bronchioles and alveolar ducts. Sometimes croupous casts of the smaller bronchi are formed.

We alluded in Art. 204 to the fact that KLEBS, KOCH, and FRIEDLÄNDER had observed the presence of micrococci in true croupous pneumonia. More recent investigations by FRIEDLÄNDER, FROBENIUS, and others make it not improbable that these micro-organisms (round or oval diplococci surrounded by a gelatinous capsule) are in causal elation to the disease. If this be established the view long maintained by JÜRGENSEN—that croupous pneumonia is the symptom of a specific infective disease—will be confirmed. The clinical course, the definite duration of the accompanying fever, and the occasional epidemic character of the disease—all point in this direction.

In addition to this idiopathic form croupous pneumonias sometimes appear in the course of various infective diseases such as malarial fever, erysipelas, and

typhoid, and in acute rheumatism. According to E. Wagner these forms have probably no ætiological connection with the first, but are due to the action of the specific poisons of the respective primary affections.

References:—Art. 204; Eberth, *Deut. Arch. f klin. Med.* XXVIII.; Friedländer, *Fortschritte d. Med.* 1883, *Virch. Arch.* vol. 87; Jürgensen, *Ziemssen's Cyclop.* v., and *Die croupöse Pneumonie* Tübingen 1884; E. Wagner, *Deut. Arch. f. klin. Med.* XXXIII; Salvioli and Zäslein, *Cent. f. med. Wiss.* 1883; Heitsch, *Ueb. infect. Pneumonie* In. Diss. Leipzig 1883; Mendelsohn, *Die infect. Natur d. Pneumonie, Zeitschr. f. klin. Med.* VII.; Ziehl, *Cent. f. med. Wiss.* 1883; Günther, *Zeitschr. f. klin. Med.* 1883 (micrococci in living patient); Discussion, *Congress f. innere Med.* Wiesbaden 1884; *Collective Investigation Record* II. London 1884; Dreschfeld, *Brit. Med. Journ.* 1, 1884, *Fortschritte d. Med.* III. 1885; Klein, *Micro-organisms and Disease* London 1884; Emmerich, *Fortschritte d. Med.* 1884; Peljesz, *D. Arch. f. klin. Med.* XXXV.; Senger, *Arch. f. exp. Path.* XX.; Cornil and Babes, *Les bactéries* Paris 1885; Sternberg, *Amer. Journ. med. sci.* 1885; Discussion, *Brit. Med. Journ.* 2, 1886.

The composition of the exudation varies much in different cases. We have already remarked that the number of extravasated red corpuscles is by no means constant; the white cells and the amount of fibrin formed is also variable. In the pneumonia of aged patients the fibrin is often scanty, so that the exudation has rather the character of inflammatory œdema, and only in isolated spots is firmly solidified. The like happens now and then in younger persons, and is indicated by the rapidity with which the affected regions recover and again contain air. It appears also that in certain cases the process may stop short at the stage of congestion, the commencing exudation being rapidly re-absorbed. The time at which hepatization is complete is also to some extent variable, so that no definite statement can be made as to the precise duration of each stage. All we can say is that during the first two days the hepatized lung is red in tint, after that it becomes pale. Sometimes the transition takes place irregularly, the lung showing patches of grayish-red, grayish-white, and yellow simultaneously.

603. As the coagulated exudation liquefies its removal becomes possible. This takes place chiefly by re-absorption, in part also by expectoration. During this process the lung appears as if saturated with moisture; it is beset with leucocytes but not in excessive number, and its tissue is easily torn.

In the great majority of cases complete recovery takes place, so that after re-absorption is complete nothing remains of the affection. The time required to bring this about varies much in different cases. Not infrequently there is for weeks some dulness to percussion over the affected region.

In few cases does any permanent textural change remain, but it is possible for the pneumonic exudation to issue in gangrene, suppuration, or cirrhosis of the lung.

Gangrene of the lung occurs when the pulmonary vessels are so gravely injured that the circulation comes to a stand-still, while putrefactive organisms gain access to the affected parts. The former condition is most frequently met with in drunkards and ill-nourished persons, in whom the pneumonic exudation often has a hæmorrhagic character. The latter condition is most likely to arise in cases where before the

attack of pneumonia bronchiectases or other cavities containing decomposing secretion exist in the lung.

The destruction of the lung may take place in isolated patches or continuously. The tissue is transformed into a tindery or pulpy mass with a characteristic intensely fœtid odor. When a gangrenous patch lies immediately beneath the pleura the latter may be raised up in bullæ or blisters, or the softened mass may break through into the pleural cavity.

The tissue surrounding the gangrenous part is inflamed and infiltrated, often hæmorrhagic. Death usually ensues either from intense pleurisy or from putrid poisoning. If recovery takes place, the gangrenous portion is separated off from the healthy by a zone of granulations, and gradually removed: in most cases a cavity remains which may be the starting-point for fresh inflammatory mischief.

Another and comparatively uncommon issue is in **suppuration,** due to excessive extravasation of leucocytes in the later stages of the pneumonia. Sometimes patches of necrosis are the starting-point of the suppuration. The accumulation of leucocytes appears partly in the alveoli, partly in the substance of the lung-tissue, and may be disseminated or diffuse. The tissue becomes yellow and very brittle; here and there it may break up and dissolve outright. Large abscesses are however very rare indeed, and are probably formed only where some previous morbid alteration has already existed.

The pus thus formed may find an exit in various directions. Most frequently it is evacuated through the bronchi. Death is a common termination; though the suppurative process may come to an end and granulations spring up, by which cicatrization is effected, or a cavity bounded by new-formed connective tissue remains.

The frequency of gangrene, suppuration, and caseation as terminations of pneumonia is still matter of discussion. LEYDEN doubts whether a lung previously healthy ever becomes gangrenous or suppurates after pneumonia. It is however by no means always possible to demonstrate *post mortem* the presence of previous morbid change. It is to be doubted whether croupous pneumonia ever issues in caseation.

References:—JÜRGENSEN, *loc. cit.*; LEYDEN, *Sammlung klin. Vorträge* 114, 115, *Deut. Zeitschr. f. klin. Med.* II.; BUHL, *Lungenentzündung, Tuberculose und Schwindsucht* 1872, *Arbeiten a. d. path. Inst. zu München* 1878; THOMAS, *Gerhardt's Handb. d. Kinderkrankh.* III.

604. Another termination of croupous pneumonia, not very common it is true but by no means rare, is in collapse and induration of the lung, a condition which is best described as **simple cirrhosis.**

In some cases this comes about by the lung failing to expand after the resolution and absorption of the exudation. This may be due to persistent obstruction of the bronchi (Art. 592, Fig. 221) or to compres-

sion from without. The walls of the unexpanded alveoli soon become coherent and undergo a certain amount of thickening.

In other cases the absorption of the exudation is incomplete: weeks and months elapse and the consolidation does not disappear. The inflammatory condition is maintained, repeated extravasations of cells from the blood-vessels into the alveoli take place, and the lung-tissue itself is the seat of inflammatory infiltration. In process of time new fibrous tissue is formed both within the alveoli and in the interalveolar septa (Art. 598, Fig. 228). In this way more or less extensive fibroid induration of the lung takes place: in many places it is transformed into a dense airless mass of fibrous tissue, usually containing pigment (Fig. 230); in other parts the alveolar walls are thickened (*b*) or infiltrated

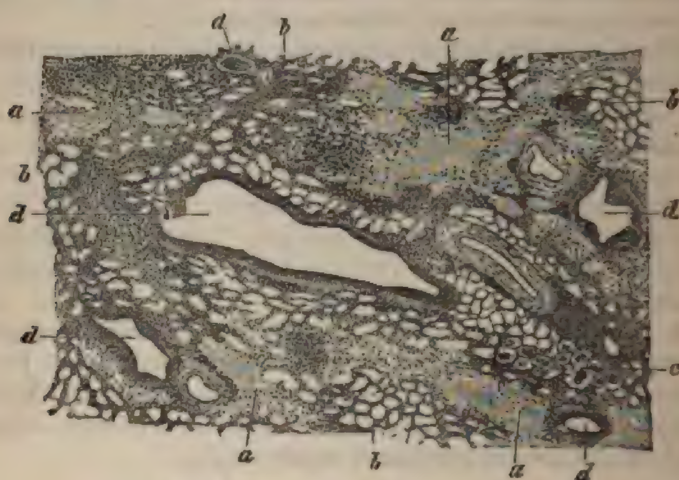

FIG. 230. SIMPLE CIRRHOSIS OF THE LUNG.

(*Hardened in alcohol and stained with carmine*: × 15.)

a, dense pigmented fibrous tissue
b, alveoli with thickened and infiltrated septa
c, alveoli filled with cells
d, dilated bronchi with infiltrated walls

with cells, or the alveoli are filled with leucocytes or new-formed cellular tissue (*c*).

The cirrhotic patches have in the earlier stages a gray or grayish-red or grayish-yellow tint, and a small quantity of turbid exudation can here and there be squeezed from them. But where the development of fibrous tissue in the alveoli or their walls has begun, the lung is dense, firm, airless, and fleshy, having something of the appearance of freshly hepatized lung. The condition is well described as **carnification.** When the fibroid transformation is complete the tissue is firm and continuous, and white or slaty-gray in color.

The extent of the induration left by an antecedent pneumonia varies very greatly. It may be limited to the stratum immediately beneath the

pleura, or extend over the greater part of a lobe. It may be continuous, that is uninterrupted by islands of air-containing tissue, or it may take the form of fibrous bands traversing the parenchyma in various directions and not very sharply marked off from it. This variety of cirrhosis is indeed always characterized by the peculiarity—that it occurs not in well-defined nodes or groups of nodes, but in bands and patches which pass gradually into the air-containing tissue. This character is obscured only when secondary bronchopneumonia or peribronchial inflammation sets in.

The pleura overlying the cirrhotic patches is usually thickened and adherent to the costal pleura. The patches are usually shrunken and contracted, and the intervening alveoli emphysematous. After a time, if the induration and contraction are at all extensive, the corresponding bronchi are distorted and more or less dilated (Fig. 230 *d*); sometimes they are also ulcerated. For months and it may be years a chronic inflammation of the bronchi and of the pulmonary parenchyma is kept up, its existence being indicated by the patches of cellular infiltration that lie scattered throughout the affected region.

The occurrence of indurative contraction of the lung as a sequel of croupous pneumonia is regarded by most authorities as indisputable. BUHL however maintains that the form of pneumonia which leads to contraction is *ab initio* distinct. According to him it begins with cellular infiltration of the parenchyma of the lung, and the filling of the alveoli with desquamated epithelium, and issues in cirrhosis and caseation. He names it 'desquamative pneumonia' and considers it as a local manifestation of a general disease. This desquamative pneumonia is not however a pathological entity: BUHL'S cases were partly cases of croupous pneumonia, partly of tuberculous, lobular, and confluent bronchopneumonia (Arts. 606, 617).

Within the last ten or twelve years ZIEGLER has had the opportunity of examining a large number of cases of post-pneumonic cirrhosis in various stages of development, and the account in the text is drawn up from actual observation. MARCHAND'S account agrees in the main with the above, though he has laid somewhat exclusive stress on the intra-alveolar formation of fibrous tissue.

References:—LAENNEC, *Traité de l'auscultation médiate* Paris 1819; ROKITANSKY, *Path. Anat.* III.; FÖRSTER, *Path. Anat*; HESCHL, *Prag. Vierteljahresschr.* vol. 51; EPPINGER, *ibid.* vol. 125; MARCHAND, *Virch. Arch.* vol. 82; BIERMER, *Virchow's Handb. d. spec. Path.* V.; BUHL, *loc. cit.*; JÜRGENSEN, *Die croupöse Pneumonie* Tübingen 1883; THOMAS, *Gerhardt's Handb. d. Kinderkrankh.* III.; LÉPINE, *Nouveau Dictionnaire* XXVIII. Paris 1880; LEYDEN, *Berl. klin. Woch.* 1879; E. WAGNER, *Deut. Arch. f. klin. Med.* XXXIII.; NOTHNAGEL, *Sammlung klin. Vorträge* 66; AMBURGER, *Deut. Arch. f. klin. Med.* XXXIII.; BASTIAN, *Reynolds' Syst. of med.* II. London 1876; STURGES, *Pneumonia* London 1876; COUPLAND, *Trans. Path. Soc.* XXX. 1879; HEITLER, *Wien. med. Woch.* 1884.

605. **Embolic septic pneumonia** always occurs in isolated patches, whose appearance varies in different cases. When infective matters enter the circulation from a septic wound, some may be arrested in the lung and give rise to embolic infarction. Suppurative inflammation is

set up around the infarcted tissue, by means of which the latter is surrounded by a zone of yellowish infiltration, and presently is loosened and separated from the healthier tissue. It then naturally undergoes necrosis and breaks up under the action of continued suppuration, so that at length there is formed a cavity filled with pus, a **metastatic abscess** of the lung. If the septic embolus contain putrefactive organisms, or if these enter the infarct from the bronchi, the tissue may undergo putrid change or gangrene, and so be transformed into a foul dirty-gray or blackish mass.

When the original irritant reaches the vessels of the lung in the form of fine particles, such as micrococci, which are not arrested till they reach the capillaries and there lodge, the patches of inflammation are usually small and ill-defined. At first the inflammation is as a rule hæmorrhagic in character, but no infarct is formed and the patches speedily become purulent or gangrenous.

In recent cases the tissue appears saturated with blood-corpuscles and pus, the pulmonary epithelium desquamated and partially necrosed. In the gangrenous patches the lung-tissue is disintegrated and dissolved (Art. 598).

When the septic embolism is subpleural, the pleura is always simultaneously inflamed. The exudation is purulent or fibrino-purulent, and may extend over the entire surface of the membrane.

Within the lung the suppuration and gangrene may extend by continuity to the neighboring tissue. The inflammation set up is usually hæmorrhagic and fibrinous in character, and speedily passes into suppuration and gangrene. Sooner or later the process reaches the peribronchial and interlobular lymphatics, and they become filled with serous, fibrinous, and purulent exudations, while the tissue about them becomes infiltrated with cells. This lymphangitis and perilymphangitis may start either from an embolic abscess or from a purulent pleurisy. In the latter case the interlobular tissues are the most affected.

The embolic abscesses may break through either into bronchi or into the pleural cavity, the former being the commoner event. When adhesions unite the lung to the thoracic wall or to the diaphragm, the pus may find its way to the exterior or into the abdomen.

The smaller abscesses may heal up more or less perfectly by absorption of the pus, the larger by rupture and evacuation; granulations are formed round the cavity, and develop into cicatricial tissue. If the absorption of the pus is incomplete it may become inspissated and calcified. Adhesions are invariably the result of the healing of the pleuritic patches.

JÜRGENSEN and SCHÜPPEL have raised the question whether the cattle-disease called **pleuro-pneumonia** does not also occur in man (WIEDERMANN, *Deut. Arch. f. klin. Med.* XXV.; SUSSDORF, *Die Lungenseuche d. Rindes* In. Diss. Tübingen 1879; BRUYLANTS and VERRIERS, *Bull. de l'acad. belgique* 1880; PÜTZ, *Seuche-*

und Herdekrankheiten Stuttgart 1882; POELS and NOLEN, *Cent. f. med. Wiss.* 1884; KORÁNYI and BABES, *Pest. med. chir. Presse* 1884; CORNIL and BABES, *Les bactéries* Paris 1885). This is an infective disease of bovine cattle, the main symptom being an affection of the lung characterized by red hepatization with extensive interlobular and pleural inflammation. The lobules appearing red and the swollen and infiltrated interlobular septa yellow, the surface has a typically marbled appearance. The exciting virus is probably a micrococcus.

The septic (suppurative and gangrenous) inflammations of the lung which occur in new-born infants are in general bronchopneumonias due to aspiration of decomposing genital secretions or liquor amnii; sometimes they are due to embolic infection from the unhealed stump of the umbilical cord. The pleura and interlobular septa are usually much inflamed at the same time.

References :—P. MÜLLER, *Gerhardt's Handbuch d. Kinderkr.* II.; ORTH, *Arch. d. Heilk.* XIII.; RUNGE, *Zeitschr. f. Geburtshülfe*, VI. (1881); SILBERMANN, *Deut. Arch. f. klin. Med.* XXXIV., and *Die septische Pneumonie d. Neugeborenen* In. Diss. Breslau 1883.

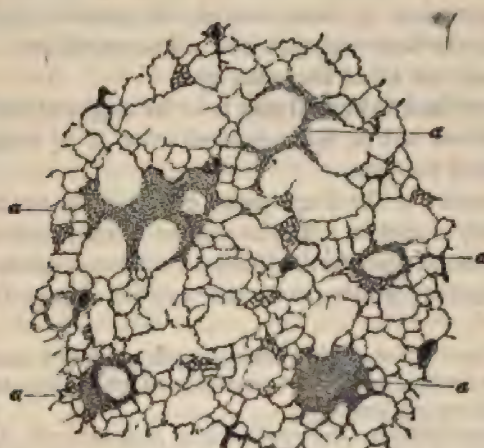

FIG. 231. MILIARY TUBERCULOSIS OF THE LUNG.

(*Preparation injected, and stained with carmine :* × 80.)

a, a, tubercles.

606. **Embolic tuberculosis** of the lung occurs in two forms. The commonest and best-known is miliary tuberculosis, the rarer is the embolic localized form.

Miliary tuberculosis of the lung is set up when tubercle-bacilli enter the circulation in considerable numbers, and lodge in the pulmonary capillaries. As they settle and multiply they give rise to the formation of miliary nodules or tubercles, which are numerous or scanty according to the number of bacilli introduced. Usually they are distributed pretty uniformly through the parenchyma of the lung and the pleura, though sometimes they are concentrated more closely in one part.

The formation of the tubercles begins with a localized cellular infil-

tration in the alveolar septa (Fig. 231) or other element of the pulmonary tissue where the bacilli have found a nidus.

The recent tubercles have all sorts of irregular shapes—crescentic, annular, stellate, and so on. Later on an accumulation of cells takes place in the neighboring alveoli and ducts and the nodules become more rounded, though even in this stage they frequently have processes and projections corresponding to the thickened alveolar septa. Where a tubercle forms the capillary-system of the part is always destroyed, so that a fully-developed tubercle is non-vascular.

Recent (or 'crude') tubercles are gray and translucent; afterwards they become opaque, yellow and caseous.

The eruption of the tubercles is sometimes accompanied by a catarrhal exudation.

A lung studded with miliary tubercles is generally hyperæmic; it is firmer and contains less air than normal, the smaller nodules are gray and translucent, the larger opaque and white or yellow. The tubercles are thus obviously not all of the same age.

Embolic localized tuberculosis is in its origin of the same nature as the miliary form, but is distinguished from it by occurring only in one or two isolated patches.

The development of the single patch corresponds to that of the disseminated miliary eruption. As the patient usually survives for a longer time, the tubercles as they form coalesce into large nodular formations which are the starting-points for further morbid change (Art. 612).

Many writers have maintained the existence of a form of lobar pneumonia of which the regular termination is in caseation, and which they consequently describe as caseous lobar pneumonia.

BUHL (*Lungenentzüdung, Tuberculose und Schwindsucht* Munich 1872) has asserted that this caseous pneumonia is a sequel of what he calls true desquamative pneumonia. This latter begins acutely like croupous pneumonia and terminates in recovery, or after weeks, months, or years, in death. The gravest form ends in caseation and is the local expression of a 'tuberculous constitution.' As we have pointed out in Art. 604, there is no distinct form of pneumonia possessing the characters which BUHL describes, and the same holds true for the so-called 'caseous labor pneumonia.' What has been so frequently described under this head is a confluent caseous lobular bronchopneumonia *of* tuberculous origin. ZIEGLER has examined a large number of lungs clinically described as the seat of caseous lobar pneumonia, and has always found them to be examples of nodular and lobular bronchopneumonia. NAUWERCK and KOCH have demonstrated the presence of tubercle-bacilli in the diseased foci (NAUWERCK, *Deut. med. Woch.* 18, 1883; KOCH, *Mittheil. a. d. k. Gesundh.* II. 1884). For an account of the various views on the subject of caseous lobar pneumonia see SHEPHERD, *Brit. Med. Journ.* 1876; HAMILTON, *ibid.* 1880; ORTH, *Lehrb. d. spec. Path.* II. Berlin 1883.

607. **Syphilitic pneumonia** occurs most frequently as the result of congenital syphilis, rarely in the acquired disease.

As we have already seen (Art. 128), when the poison of syphilis is

diffused by way of the circulation it sets up inflammations which in some cases differ little from ordinary non-specific forms, in others are characterized as specific by the formation of gummatous foci. Both forms occur in the lung, but are certainly very rare indeed (if we except congenital syphilis), and this specific character is by no means easily established.

Gummatous pneumonia is a syphilitic inflammation of the lung in which caseous granulomatous foci develop within patches of inflamed pulmonary tissue or of new-formed and hyperplastic fibrous tissue. Similar foci are often described as met with in post-mortem examinations, but there is little doubt that in most cases they are not due to syphilis. They are in general merely encapsulated patches of bronchopneumonia, dilated bronchi filled with caseous exudations, caseous detritus lying within dilated and thickened lymphatics and surrounded by new-formed fibrous tissue, and so on.

Gummata are extremely rare in the lungs of adults; they are commoner in new-born syphilitic infants, and may occur in considerable numbers. When recent, they are gray or grayish-white and somewhat translucent; they vary from the size of a pea to that of a hazel-nut. Afterwards the centre becomes white and opaque, and by disintegration may even become excavated.

Another form of syphilitic pneumonia in infants gives rise to diffuse cellular inflammation of the lung, often accompanied by desquamation and fatty degeneration of the pulmonary epithelium. The diseased tissue is abnormally hard and white, and the affection has therefore received the name of **white pneumonia.**

Some writers describe a similar form in adults as the result of acquired syphilis, and it is said occasionally to lead to fibroid induration of the lung. According to PANKRITIUS it usually starts from the hilum and extends radially. Others describe as syphilitic certain indurative inflammations starting from the pleura or the interlobular septa.

Some of these inflammatory indurations in syphilitic subjects are no doubt due to the specific influence of the disease, but it is very difficult to distinguish them with any certainty. We may be sure that many of the indurative changes in the lung set down to syphilis have really no connection with it, but are due to other causes. The like is true of many of the so-called syphilitic cicatrices of the lung, the pleura, and the interlobular septa.

On syphilitic bronchopneumonia see Art. 618.

VIRCHOW has expressly called attention to the fact that the diagnosis of syphilitic changes in the lung is of exceptional difficulty: he thinks however that both gummatous and simple irritative inflammations of the lung due to syphilis do occur. Among the latter are certain forms of fibrous pneumonia, pleurisy, and peribronchitis, and of catarrhal and caseous bronchopneumonia. Although of late years much has been published on the subject of pulmonary syphilis it

[illegible] knowledge of its morbid anatomy has much advanced. [illegible] leave room for considerable doubt as to their syphi- [illegible]

[illegible] *Gaz. des hôpitaux* 1851; HECKER, *Virch. Arch.* vol. 17, [illegible] VIII. (1854); E. WAGNER, *Arch. d. Heilk.* IV. (1863); [illegible] *Zeitschr.* IV. (1863); VON BÄRENSPRUNG, *Hereditäre* [illegible] VIRCHOW, *Virch. Arch.* vols. 1 and 15, *Krankhafte Ge-* [illegible] BOWITS, *Arch. f. Syphilidologie* III.; ANDREAE, *Anat.* [illegible] *Kinder* In. Diss. Würzburg 1875; SCHÜTZ, *Syphilome* [illegible] *z. path. Anat.* I. 1878; VIERLING, *Deut. Arch. f. klin.* [illegible] *Arch. f. Derm. u. Syph.* V. (1878); PAWLINOFF, *Virch.* [illegible] SCHNITZLER, *Die Lungensyphilis* Vienna 1880; GRANDIDIER, *Berl.* [illegible] GERHARDT, *Sitzungsber. der phys.-med. Gesellsch. z. Würzburg* [illegible] *d. Heilk.* XIX.; THOMPSON, *Lancet* 1, 1878; SACCHARJIN, [illegible] TIFFANY, *Amer. Journ. med. sciences* 1877; PANKRITIUS, [illegible] Berlin 1881; GÜNTZ, *Memorabilien* 1882; CORNIL and RAN- [illegible] London 1884; KOPP, *Deut. Arch. f. klin. Med.* XXXIII.; [illegible] 1884 (with critical summary of published cases); [illegible] *path. Anat.* II. 1884; GOODHART and others, *Trans.* [illegible]

[illegible] **Pleurogenous pneumonia.** When the pleura becomes af- [illegible] (pleurisy) the underlying pulmonary tissue [illegible] mechanically (Art. 591) or by extension of the [illegible] to the lung. The extension takes place chiefly by [illegible] which are very abundant in the pleura and com- [illegible] those of the interlobular septa. The first sign of [illegible] into the lymphatic vessels, by which they [illegible] the dimensions of a middle-sized bronchus.

[illegible] of this kind may result from various types [illegible] it is most commonly associated with purulent [illegible] pleurisy, whether set up by pyæmic (embolic) suppu- [illegible] or as a primary local affection. For example, it is [illegible] met with in infants who have died of pyæmia from sep- [illegible] umbilicus.

[illegible] of the interlobular lymphatics with purulent or [illegible] causes the lobules to be separated by zones of [illegible] tissue, and if the septa themselves undergo [illegible] may be loosened and isolated from each other. [illegible] inflammation is accordingly spoken of as dis- [illegible] (HUTINEL and PROUST, *Archives générales de* [illegible]

[illegible] the inflammation may spread to the peribronchial [illegible] them in a similar way. The lobules also may [illegible] so that the already compressed lung-tissue becomes [illegible] exudation and infiltration—catarrhal, croup- [illegible] or purulent—as the case may be. Accordingly the [illegible] grayish-red, or grayish-yellow, and saturated with

a turbid secretion. The appearance of the lung is in fact like that of an ox dead of pleuro-pneumonia (Art. 605).

If the disease is not fatal, recovery takes place by resorption, though in most cases there remains some permanent thickening of the interlobular tissues. Should residues of inspissated pus remain in the thick-

FIG. 232. CHRONIC PLEUROGENOUS INTERLOBULAR PNEUMONIA.

(*Hardened in Müller's fluid, stained with picrocarmine;* × 3.5.)

a, thickened pleura
b, pulmonary tissue
c, thickened interlobular septa
d, cellular infiltration at the boundaries of the thickened septa
e, dilated bronchus with infiltrated mucous membrane *f* and thickened peribronchial tissue
g, bronchioles with infiltrated walls

ened septa, nodules having much resemblance to gummata are formed and have occasionally been mistaken for them.

Tuberculosis may in like manner extend from the pleura to the lung, as in cases of tuberculous disease of the ribs or vertebræ; and then tubercles appear along the course of the several lymphatics.

Chronic indurative and plastic inflammations of the pleura may also extend to the alveoli by way of the interlobular and peribronchial channels.

The thickening of the pleura causes the lung to be enclosed in a thick, tough, fibrous casing (Fig. 232 *a*) from which stout fibrous bands (*c*) (corresponding to the interlobular septa) extend into the pulmonary tissue, forming a kind of coarse meshwork with the thickened peribronchial tissue (*e*).

The pulmonary tissue enclosed in the meshes of the septa is more or less compressed, and sometimes becomes entirely collapsed and functionless. Moreover active inflammation may extend from the septa to the alveoli (*d*) and give rise to infiltration and fibrous hyperplasia in them. Very frequently too the morbid process is associated with evidences of bronchopneumonia, either primary, secondary, or antecedent.

The bronchi of the affected region seldom remain entirely healthy. As a rule they are distorted and dilated (*e*), partly owing to the traction of the shrinking fibrous tissue, partly to the pressure of the air which is irregularly distributed among the alveoli. There is usually also some bronchial catarrh, the mucous membrane both of bronchi (*f*) and bronchioles (*g*) being visibly infiltrated.

609. **Inflammation of other contents of the thorax** or of the abdomen sometimes extends to the lungs. The mediastinal organs, the bronchial glands, the œsophagus, the stomach, and the liver, are the parts most commonly concerned. And according to the character of the primary affection the inflammation of the lung may be purulent or putrid, tuberculous, caseous, or indurative. Thus a tuberculous gland may give rise to tuberculosis of the root of the lung, and an abscess of the liver breaking through the diaphragm may cause suppuration of the base of the lung with purulent pleurisy or empyema.

In ulcerative disease of the lung the bronchi may become perforated. A basal abscess, for instance, or a broken down caseous bronchial gland, may rupture into a neighboring bronchus. If the matters thus evacuated are infective or irritating, and if some of them are aspirated into other parts of the parenchyma of the lung, secondary bronchopneumonia may result (Art. 613).

Traumatic lesions of the lung, caused for example by a fractured rib, give rise in the first place to hæmorrhage and perhaps entrance of air into the pleural cavity (pneumothorax). If the wound is not contaminated the rent is healed by thrombosis and subsequent cicatrization. Septic contamination of the wound results in suppuration and gangrene of the lung.

CHAPTER LXXXVII.

FORMS OF BRONCHOPNEUMONIA.

610. **Non-specific bronchopneumonia.** All forms of bronchopneumonia are at first essentially local disorders, whose extent and distribution are determined by the position and relations of the affected bronchioles and alveolar ducts. This local character is most apparent when the irritant substance which induces the bronchopneumonic inflammation is in a minutely divided form and suspended in the inspired air, so that it reaches the terminal air-passages directly. In animals such inflammations can readily be produced by causing them to breathe an atmosphere containing irritant substances in the form of dust

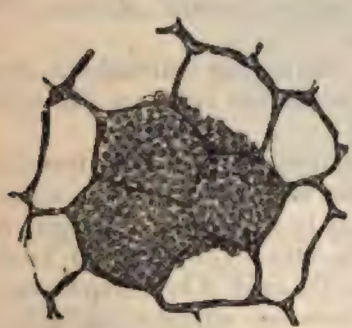

FIG. 233.

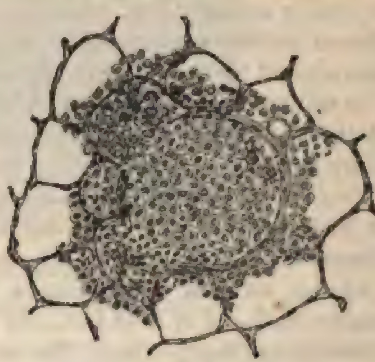

FIG. 234.

FIG. 233. MILIARY BRONCHOPNEUMONIA.

A patch extending over three alveoli.

(*From the lung of a dog, after inhalation of an irritating spray*: × 30.)

FIG. 234. MILIARY BRONCHOPNEUMONIA.

A patch extending over a respiratory bronchiole and the adjacent alveoli: some of the extravasated cells contain particles of dust.

(*From the same lung.*)

or spray. In man the earlier stages can be observed only in cases where shortly before death a quantity of irritating dust, or very small particles of secretion from the air-passages themselves, have been inhaled.

Wherever these particles lodge an acute reactive inflammation is set up around them, first of all in the wall of the particular air-space, and soon (if the irritation be sufficiently great) in the adjoining tissue also.

In this way are formed minute, or as they are called miliary, patches of inflammation starting from the terminal air-sacs or infundibula (Fig. 233), or from the alveolar ducts and respiratory bronchioles (Fig. 234) with their alveoli, and spreading to the neighboring elements by direct extension.

When the aspirated substances are still more irritating (*e. g.* saliva with remains of food, pus from laryngeal abscesses, etc.), the inflammations induced are more extensive. In this way are produced larger areas of bronchopneumonia extending over a number of contiguous alveoli, alveolar ducts, and bronchioles. When entire lobules are thus attacked we have what is called **lobular bronchopneumonia.** When all or most of the lobules of a lobe are simultaneously affected we have what may be called **lobar bronchopneumonia.**

The appearance of the bronchopneumonic patches naturally varies with the form of the inflammation (Arts. 596, 597) and the stage it has reached. When exudation has followed upon the initial hyperæmia, the spots have a dark-red, grayish-red, gray, or grayish-yellow tint, and yield on pressure a turbid liquid whose tint varies in like manner, according to the proportion of red and white blood-cells it contains. Only in croupous inflammations is the exudation solid or semi-solid and not readily squeezed out. The cut surface has a granular look. The inflamed patches are sometimes well-defined, sometimes indistinct. The tissue around them is usually hyperæmic.

In miliary bronchopneumonia when the cellular infiltration is dense and the patches sharply-defined, they sometimes look very like recent miliary tubercles.

Very frequently indeed bronchopneumonia is preceded by bronchitis and bronchiolitis, and thus before the respiratory tissue is actually inflamed some of the smaller bronchi may be obstructed and so give rise to lobular collapse or atelectasis (Art. 591). The collapsed lobules assume a dark-red or livid tint, and thus the onset of bronchopneumonia in them is not very obvious. The tint alters only after a certain amount of cellular and serous exudation has taken place into the alveoli, and then the characteristic turbid juice can be squeezed from the affected tissue.

611. The **number and distribution** of the bronchopneumonic centres will of course be very different in different cases. In one instance they may be scattered over both lungs, in another confined to a part of a single lobe. When a large number of lobules are collapsed or inflamed, compensatory dilatation of the still active lobules takes place. Subpleural inflammations usually lead to inflammation of the pleura also.

Suppuration and gangrene of the bronchopneumonic patches are comparatively infrequent; they are most commonly due to the aspiration of irritating liquids from the mouth or stomach, or of pus and detritus from abscesses or ulcers in the larynx or trachea, from cavities

in the lung itself, and so on. As in the case of embolic abscesses and necroses, these **bronchopneumonic abscesses** may heal more or less completely by delimiting inflammation and cicatrization. Death however is the more frequent result.

In most cases of bronchopneumonia the exudation is absorbed, and the lung restored to its normal state. It must however be remembered that unabsorbed residues are much more common after bronchopneumonia than after croupous pneumonia. Even in the non-suppurative forms the cellular infiltration of the interlobular and peribronchial fibrous structures is here and there so abundant that complete resorption is impossible: the circulation of the part may indeed be so much interfered with that caseous necrosis takes place. In other cases the inflammation persists for a considerable time, and passing into a chronic condition leads to the formation of new fibrous tissue and thus to induration.

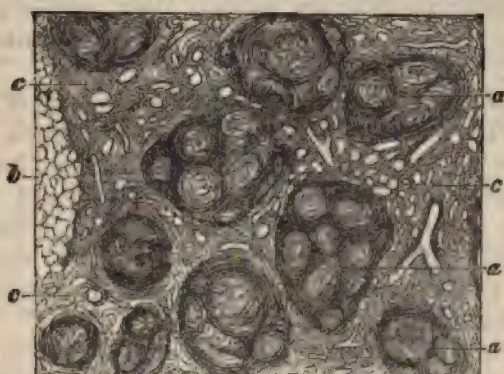

FIG. 235. MASON'S LUNG WITH BRONCHOPNEUMONIC FIBROUS NODULES.

(Section hardened in alcohol, and stained with picrocarmine: × 9.)

a, group of fibrous nodules
b, normal pulmonary tissue
c, thickened pulmonary tissue containing bronchi, vessels, and a few alveoli

Dry **caseous necrosis** of the pulmonary tissue occurs generally as a sequel of the lobular inflammation, especially in children suffering from bronchitis and bronchopneumonia after measles or whooping-cough. It may however occur in adults and in connection with other forms of bronchopneumonia. While many of the patches of inflammation disappear by resorption, here and there the exudation persists, condenses, and by degrees assumes a dry cheesy consistence, while the surrounding tissue simultaneously undergoes necrosis. In this manner caseous nodules, from the size of a pea to that of a walnut, are produced; after a time they become enclosed in a fibrous capsule, and then may remain for an indefinite time without further change, though frequently they become calcified. These nodules are met with in all parts of the lung,

though the apex is the commonest seat. Occasionally they give rise to obstruction of some of the bronchial tubes (Art. 580).

A more frequent result of bronchopneumonia is induration or **cirrhosis of the lung.** In its least-complicated form this occurs in cases where the continual inhalation of irritating dust keeps up a constantly-renewed inflammation.

Coal-dust is the least irritating, stone-dust and metallic particles are much more injurious. The power of the absorbents is usually insufficient to remove all the dust inhaled, and inflammation being set up around the particles that remain in process of time they are enclosed in capsules of new fibrous tissue (Fig. 235 *a*), and thus give rise to hard fibrous nodules.

In some cases these nodules are few and scattered: in others they are numerous and lie together in groups (Fig. 235). Instances occur in which they are so numerous in particular parts of the lung that scarcely any air-containing tissue exists between them, and in other parts the lung is entirely fibrous. This condition is best described as **nodular cirrhosis.**

The separate nodules are of various sizes from that of a lentil to that of a bean. They are white, slate-colored, or even black, and that even in the absence of coal-dust. The pigment is then derived from the coloring-matter of the blood. When fully developed they consist of coarse fibrous tissue, often concentrically stratified. Larger nodes are formed by the coalescence of smaller nodules, and correspond to the territory of a single bronchiole: the smallest nodules represent terminal alveoli or infundibula.

The tissue round about the nodules is infiltrated with cells, or thickened and fibrous, the indurative inflammation extending radially.

When the bronchopneumonia is lobular, and associated with obstructive collapse, the nodular cirrhosis is accompanied by a more diffuse indurative change, which we may call **lobular cirrhosis.** In this way, as in the cirrhosis of simple collapse (Art. 592, Fig. 221), the lung is beset with patches of compact gray or slate-colored tissue, enclosing scattered nodules which are usually of a paler tint.

Patches of this kind may be formed in any part of the lung, though they are most common at the apex: not infrequently they contain small cheesy nodules.

The pervious bronchi traversing the indurated region generally become dilated, and are the seat of chronic inflammation often of an ulcerative kind and leading to the formation of cavities or **vomicæ.** When such a vomica contains a decomposing or irritant secretion, the latter may gain access to the air-passages and by aspiration pass into the terminal branches of other bronchi. In this way fresh bronchopneumonia is set up, and may lead to miliary or nodular or lobular inflamma-

tion, ending in local recovery, or it may be in suppuration or induration like the first.

The pleura is affected in all bronchopneumonic indurations that are not entirely limited to the deeper parts of the lung; thickening and adhesions are the usual result. So also it is not unusual to find thickening of the peribronchial and the interlobular fibrous tissue.

612. **Tuberculous bronchopneumonia.** Tuberculosis of the lung may begin in one of three ways: namely, as embolic tuberculous pneumonia, as primary tuberculous bronchopneumonia, and as tuberculous lymphangitis.

Embolic tuberculous pneumonia has already been considered (Art. 606). It takes the form either of disseminated miliary tuberculosis and terminates fatally, or of a localized affection leading to the formation of one or more isolated caseous nodes. These nodes may occur either in a part of the lung previously healthy, or in tissue already altered by disease.

Tuberculous lymphangitis (Art. 609) takes the form of a local eruption of tubercles in the neighborhood of a tuberculous focus outside the lung. A caseous bronchial gland or tuberculous disease of the vertebral column is the commonest starting-point of the affection.

Primary tuberculous bronchopneumonia attacks both healthy and diseased lung-tissue.

In the former case tubercle-bacilli, either alone or accompanied by other irritant matters, gain access with the inspired air to the respiratory parenchyma, settle in some ramification of the air-passages, and in the first instance give rise to a nodular patch of inflammation (Fig. 236 *g*). Occasionally the bacilli may at once be taken up by the lymphatics and give rise first in them to the formation of granulomatous nodules.

When the tubercle-bacilli alone enter the lung, these are the only changes induced; but if at the same time other sources of irritation are at work the tuberculous changes are accompanied by more or less extensive bronchitis and bronchopneumonia. As the case goes on the latter affections pass away, often however leaving behind bronchi obstructed with secretion, or collapsed and indurated patches sometimes containing caseous foci; so that the affected part of the lung includes one or more caseous patches (*e*) containing bacilli, caseous masses free from bacilli, obstructed or occluded bronchi, and gray cirrhotic areas. In certain cases patches originally containing bacilli may become free from them, and undergo cicatrization with or without caseous enclosures.

The specific infection frequently reaches a lung already morbidly affected. If the affection is a recent bronchitis with bronchopneumonia, the after-course of the disease will resemble that just described. Exactly how often such a secondary infection takes place it is not at present easy to determine. Most probably we have instances of it in those cases

where chronic tuberculosis appears to be developed from a non-tuberculous bronchopneumonia such as follows measles or whooping-cough.

Secondary tuberculous infection is also favored by the fact that inhaled bacilli may develop more readily in tissue which is altered by antecedent or still persisting chronic inflammatory processes. This possibility is supported by the observation—that certain tissue changes connected with particular inflammatory affections of the lung appear to predispose it to tuberculosis. So far as can be made out by morbid anatomy these are chiefly—caseous necrotic patches, inspissated collections

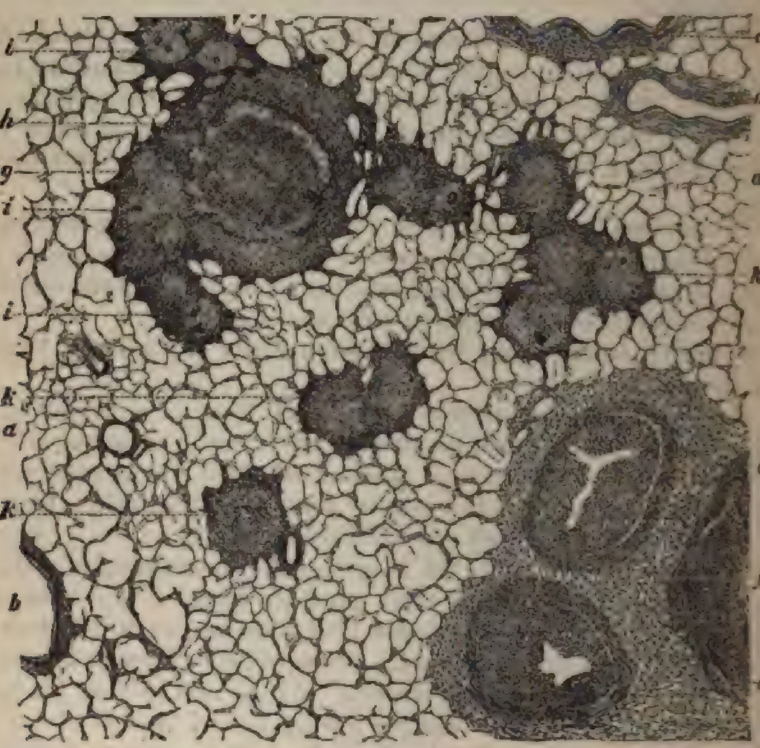

FIG. 236. PRIMARY TUBERCULOUS BRONCHOPNEUMONIA WITH COMMENCING TUBERCULOUS LYMPHANGITIS.

(*Section from the left apex of the lung of a woman of 25, which contained a few scattered nodes with central caseation; carmine staining*: × 15.)

a, normal lung-tissue
b, normal bronchus
c, bronchus with inflamed wall
d, artery
e, encapsuled caseous bronchopneumonic patches
f, fibroid induration
g, caseous centre and
h, cellular periphery of a tuberculous node
i, *k*, tubercles in the neighboring lymphatic vessels

of bronchial secretion, and bronchiectatic cavities. The predisposition does not depend on the way in which these morbid changes have been brought about. When the bacilli once gain a settlement the periphery

of the caseous node or the wall of the bronchiectatic cavity becomes the seat of a new inflammation which thenceforth exhibits the character of a tuberculous process.

The author has for a number of years endeavored from the anatomical side to make out the early stages of pulmonary tuberculosis, and the above account represents the outcome of his investigations. In Würzburg and in Zürich he had to make post-mortem examination of a large number of children and young persons, and so had frequently the opportunity of observing tuberculosis in all its stages, even from the very beginning. He has thus convinced himself that in the great majority of cases tuberculosis of the lung begins in the form of solitary nodes or nodular foci. The tuberculous nature of these foci is in general readily determined from the appearance of the parts immediately around them. Recently also NAUWERCK and GLASER have demonstrated the presence of tubercle-bacilli in some of the cases collected by the author.

The occurrence of secondary tuberculous infection in lungs already diseased appears to follow from the frequently-observed fact that recent tuberculous bronchopneumonia is found side by side with old patches of induration that are devoid of any recognizably tuberculous character, while the bronchiectatic cavities they enclose contain tubercle-bacilli. It must however be granted that a tuberculous lung may recover locally, the disease sometimes leaving behind it patches of induration that possess none of the special characters of tuberculosis.

Formerly attempts were made to explain pulmonary phthisis and tuberculosis as the direct result of a special **constitution** or predisposition, which reacted in a peculiar way to ordinary irritations. After the communicability of tuberculosis was established stress was always laid on the fact that certain animals are more susceptible of the disease than others, and accordingly the special predisposition of the individual has always been regarded as a principal factor in the genesis of tuberculosis. Since KOCH'S discovery of the tubercle-bacillus the question of predisposition has fallen somewhat into the background. It appears however unwise to lose sight of what is almost certainly the fact—that many persons are more disposed to become tuberculous than others. This predisposition is either congenital or acquired, and consists either in local alterations of tissue or in the general constitution of the system, that is in peculiarities of the metabolism of the tissues. For instance, diabetic patients are well-known to be very apt to suffer from a fatal form of tuberculous phthisis. Other predisposing conditions are—excessive smallness of the heart in proportion to the lungs and the body generally, poverty of the blood in albuminoids and water such as follows continued lactation, suppuration, cholera, etc., lesions of the heart limiting the blood-supply to the lungs, contracted thorax, and enfeebled inspiration. Scrofula, that is to say the particular anomaly of constitution which is manifested chiefly by a tendency to chronic catarrh of mucous membranes, also favors tuberculous infection. How exactly these conditions act as predisposing causes of tuberculosis we can hardly at present determine, though all clinical experience goes to show that they are of some importance.

In addition to the constitutional predisposition we have to consider the **local predisposition**: and it is reasonable to suppose that in the case of the lung this latter plays a considerable part. Thus lung-tissue that is inflamed or that is altered in a certain way by previous inflammation is more apt to become tuberculous than normal healthy tissue.

Lastly, it appears certain that many persons are predisposed or rather predestined to tuberculosis because they are much more exposed to the chances of

infection than others. This is especially the case with children who grow up in the company of tuberculous parents.

An extremely important, but at present involved, question is—whether tuberculosis can be **inherited**, *i. e.* whether the tubercle-bacillus can be transmitted from the parent to the fœtus in fecundation or during gestation. ZIEGLER has pointed out in several of his writings that no anatomical facts are yet to hand in support of the affirmative supposition. There is on record no indubitable instance of intra-uterine fœtal tuberculosis, and after birth the affection appears at the earliest in the third week, by which time it is quite possible for infection from without to have taken place. It must however be kept in mind that in some instances the disease had at this time made such progress that the beginning of it might with great probability be referred to the intra-uterine period (DEMME and LICHTHEIM, *Verhandl. d. med. Congresses in Wiesbaden* 1883). ZIEGLER'S view is—that **congenital tuberculosis** is possible but not yet certainly demonstrated, and that it must at any rate be rare. Since KOCH'S discovery a good many authorities have come over to this view. Actual transmission of tuberculosis to the fœtus appears conceivable only when at the time of impregnation the male suffers from urogenital tuberculosis, or when during gestation the female genital organs are tuberculous, or tubercle-bacilli gain access to the circulatory system. Future observation alone can determine whether this view is correct or not and meanwhile we may explain the fact—that the children of tuberculous parents so readily perish from tuberculosis—by observing that they inherit some predisposition to the disease and by their constant intercourse with the parents are in a special way exposed to the risk of infection.

Tuberculosis by **inhalation** was first induced in animals by TAPPEINER, LIPPL, and SCHWENINGER (*Naturforscherversammlung in München* 1882, *Virch. Arch.* vols. 74, 82), afterwards by WEICHSELBAUM (*Cent. f. med. Wiss.* 1882, *Wiener med. Jahrb.* 1883), SCHOTTELIUS (*Virch. Arch.* vol. 73), and others. When animals are made to breathe air containing phthisical sputa pulverized by means of the spray apparatus, small miliary bronchopneumonic patches much resembling tubercles are found in the lungs. TAPPEINER took them for actual tubercles and compared them to the tubercles found in miliary tuberculosis of the lung. This however is a mistake: they are multiple primary tuberculous bronchopneumonic patches of miliary size, caused by the inhalation of tubercle-bacilli (ZIEGLER, *Sammlung klin. Vorträge* 151). VERAGUTH worked at the subject in ZIEGLER'S laboratory during 1881-82, and showed that in the bronchopneumonic patches great masses of bacilli were developed, that in course of time from these patches were formed larger caseous and even ulcerating nodes, and that in goats the process might give rise to tuberculous disease of the lymphatics, lymphatic glands, and serous membranes, all of which contained bacilli. Fourteen days elapse from the time of inhalation before the first visible changes are detected. As the changes set in masses of bacilli are seen in the alveolar epithelial cells, which they presently cause to degenerate, while reactive inflammation is set up in the adjacent tissue.

References:—BAYER, *Études compar. de la phthisie pulmonaire* 1842; SEEGEN, *Der Diabetes mellitus* Berlin 1878; BOUCHARDAT, *De la glycosurie* Paris 1878; LEYDEN, *Ueb. diabet. Lungenphthise, Zeitschr. f. klin. Med.* IV.; RÜHLE, *Ziemssen's Cyclop.* V.; JÜRGENSEN, *ibid.*; ZIEGLER, *loc. cit.*; BAUMGARTEN, *Zeitschr. f. klin. Med.* VI., *Sammlung klin. Vorträge* 218, *Berl. klin. Woch.* 1883; *Collective Investigation Record* I. London 1883; KLEBS, Art. *Tuberculose, Eulenburg's Encyclopädie* XIII.; VERAGUTH, *Arch. f. exp. Path.* XVII. 1883; KÖSTER, *Sitzungsber. d. niederrhein. Gesellsch.* Bonn Feb. 1876; SENISE, *Movimento med. chir. di Napoli* 4, 1883; JOHNE, *Geschichte d. Tuberculose* Leipzig 1883, and *Die käsige*

Hüttenrauchpneumonie d. Rindes, *Fortschritte d. Med.* I. 1883, III. 1885; BIEDERT and SIGEL, *Virch. Arch.* vol. 98; WARGUNIN, *ibid.* vol. 96; WAHL, *Deut. med. Woch.* 1, 1885; SCHÄFFER, *Die Verbreitung d. Tuberculose in den Lungen* In. Diss. Berlin 1884; BREHMER, *Die Aetiol. d. chron. Lungenschwindsucht* Berlin 1885.

613. **Extension of tuberculosis in the lung.** The manner in which tuberculosis of the lung extends from part to part is always the same, whether the original infection is due to embolism or to inhalation.

The first-formed nodule increases in size by **peripheral extension** of the cellular infiltration. The accumulation of cells in the contiguous alveolar walls and alveoli takes place continuously and uniformly (Fig. 236 *h i*), though here and there we may find typical tubercles with epithelioid cells and giant-cells in the midst of the mass of simple leucocytes.

After a certain time this continuous extension is accompanied by **tuberculous lymphangitis**, manifested by the development of tubercles in the course of the surrounding lymphatics (Fig. 236 *i k*). This eruption may be interalveolar, interlobular, or peribronchial, and often spreads rapidly to the pleura and the bronchial glands.

In many cases this is the only mode of extension, at least for a considerable time. For months together, either steadily or with occasional pauses, fresh nodular foci continue to be formed along the course of the lymphatics, and the intervening tissue becomes chronically inflamed. In this way patches of induration of various sizes are produced, which contain single tubercles and groups of tubercles, usually all enclosing bacilli, and in various stages of growth and decay.

Sooner or later another mode of extension takes place in addition to this ordinary one of lymphangitic induration and caseation.

A primary (or it may be a secondary) caseous node reaches a certain size, softens and disintegrates, and then breaks through into a bronchus. The caseous detritus contains tubercle-bacilli, and consequently a possibility arises that the disease may be spread to other parts of the lung by **aspiration** into the air-passages. As a fact much of the detritus and the bacilli are coughed up as sputum, but some may be aspirated into the smaller tubes and so reach the respiratory parenchyma. This may also happen when the infected contents of a bronchiectasis or of a bronchiectatic vomica are emptied into a bronchus, or when a cheesy tuberculous gland softens and breaks through.

The aspirated matters lodge in various parts of the pulmonary tissue and give rise to a reactive inflammation whose extent and intensity depend partly on the amount and nature of the irritant substances, partly on the relations of the tissue involved, partly on the special predisposition of the patient. As regards the irritant substances it must be kept in mind that they often include not only tubercle-bacilli but also other micro-organisms and chemical products of decomposition from the

diseased cavities, and these may give rise to suppurative, or fibrinous, or even putrid inflammations.

In this way a fresh focus of bronchopneumonic inflammation is lit up. The course of the new inflammation is in general this—there is first an abundant cellular exudation; after some days or weeks this forms a nodular infiltrated patch (Fig. 237 *f g*), which then becomes caseous in the centre (*f*), while the periphery (*g*) consists of living cells. By proper staining-methods bacilli (*h*) can be shown lying singly or in groups both in the caseous and in the cellular parts. The vessels which

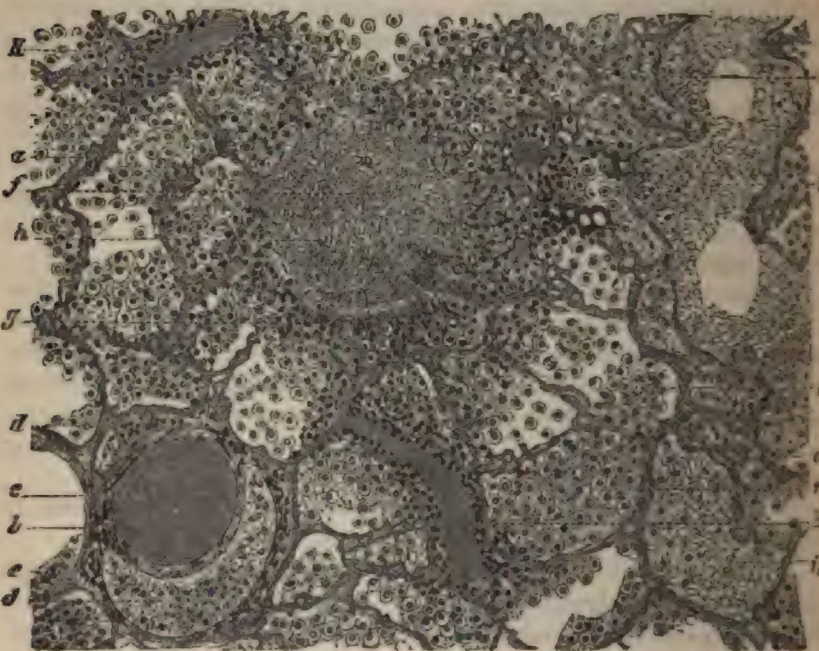

FIG. 237. MILIARY TUBERCULOUS BRONCHOPNEUMONIA.

(This is a secondary patch due to the aspiration of the contents of a small caseous node which ruptured into a bronchus: preparation injected with blue gelatine and stained with alum-carmine: the bacilli drawn from a parallel section stained with fuchsin: × 80.)

a, interalveolar septa with injected capillaries
b, respiratory bronchiole
c, injected artery
d, circumvascular lymphatic distended with exudation
e, pigment lying round the lymphatic
f, caseous centre, and
g, cellular periphery of the bronchopneumonic patch
h, tubercle-bacilli (× 160)
i, cellular exudation in the alveoli
i_1, chiefly fibrinous exudation
k, vein with surrounding cellular infiltration
l, interlobular lymphatic distended with exudation

traversed the part occupied by a solid nodule of this kind are always destroyed.

The lung-tissue around the nodule is the seat of an exudative in-

flammation, whose intensity differs greatly in different cases. As a rule the neighboring alveoli (i) contain extravasated liquid and cells, desquamated epithelium, and often fibrin (i_1). The alveolar walls are infiltrated with leucocytes, especially around the veins (k). The lymphatics, peribronchial and periarterial (d) as well as interalveolar and interlobular (l), are also in some measure affected by the inflammation, being more or less distended by exuded matters (d l). When the nodule is subpleural, the pleura is simultaneously inflamed.

When a number of tuberculous bronchopneumonic foci are thus formed by aspiration, each passes through much the same series of changes as were described in the case of the primary focus. Some continually enlarge and lead to progressive tuberculous lymphangitis, others soften and break down and by aspiration of their contents lead possibly to fresh bronchopneumonic infection.

At all stages of the disease there is still another possible mode by which the infective agent may be disseminated. Chronic inflammatory change in the lung always extends in some degree to the blood-vessels. Plastic inflammation leads to fibrous thickening of the walls of arteries and veins, and by endarteritic thickening some of the smaller branches may be obliterated altogether. In tuberculous inflammation of the lung the walls of the capillaries as well as those of the arteries and veins are especially apt to be affected. When an actual tuberculous node or nodule is formed the capillaries perish outright, while in the walls of the larger vessels appear granulomatous growths having all the characters of tubercle, and developing some into fibrous thickenings and some into caseous ulcers. These several morbid changes naturally lead to local disorders of the circulation, and to more or less copious hæmorrhages (**hæmoptysis**), which are most apt to follow when the walls of arteries are diseased and are eroded or give way. But there is also the danger that the caseous growths on the walls of veins may break into the interior of them, and permit the tuberculous detritus and bacilli to enter the circulation and spread the infection to distant organs. This however appears not to happen at all frequently, no doubt because before a tubercle actually breaks through the intima into the vein thrombosis is induced by the diseased state of the wall, and in this way the vein itself is effectually blocked up (compare CORNIL, *Journ. de l'anat.* 1880; MÜGGE, *Virch. Arch.* vol. 76; ARNOLD, *ibid.* vol. 88; WEIGERT, *ibid.* vols. 77, 87, 104).

The tubercle-bacilli may at a very early stage of the disease pass from the peribronchial lymphatics into the bronchial glands, and there set up tuberculous changes. Cases indeed not infrequently occur in which only a few scattered bronchopneumonic nodules are found in the lungs, while some of the bronchial glands are tuberculous throughout or entirely caseous. It has even been noted that only a single small patch

may occur in the lung, or that no patch at all may be discovered, and yet the bronchial glands may be extensively diseased.

After the tuberculous process has spread over a considerable part of the lung and the lymphatics the bronchi also become diseased in like manner. The smaller tubes are first affected, then the larger, and often the trachea and larynx as well. If the sputum be swallowed tuberculosis of the alimentary canal may be set up.

The author in a lecture published in 1878 (*Sammlung klin. Vorträge* 151) explicitly insisted on the fact that the extension of tuberculosis in the lung takes place by way partly of the lymphatics and partly of the bronchial passages, the whole course of the disease suggesting inevitably that the secretion and other contents of tuberculous cavities act infectively upon the sounder parts of the lung. This statement was based chiefly on the results of anatomical examination and on the experiments on inhalation cited in Art. 612. The subsequent discovery of the tubercle-bacillus, and the demonstrated fact that the sputum from the diseased lung contains bacilli, corroborate the statement, and all the author's recent observations in the post-mortem room are in entire accord with it. When a number of tuberculous bronchopneumonic patches are found in a lung, there is always present an older disintegrated focus or a bronchiectasis or a caseous lymphatic gland: in these the bacilli have multiplied and have thence been disseminated along the air-passages.

We are unable to set forth in detail the numerous and various accounts which have been given of tuberculous disease of the lung. An analysis of them could only be of value if accompanied by the arguments which have induced us to set aside those that differ from the account in the text, and this would scarcely be in place in a work like the present. In general terms it may be said that some of the views referred to are erroneous because they rest on mistaken ideas as to the structure of the lung; and further that sufficient attention has not been paid to the distinction between diseases of the respiratory parenchyma of the lung and diseases of the bronchi and peribronchial tissue. Many affections have thus been described as peribronchitic in which the peribronchial tissue is intact, the affection being really one of the respiratory tissue and only properly described as bronchopneumonic. Authors again have in many cases entirely ignored the lymphatics, while a few have exaggerated the part they play.

References on the morbid anatomy of chronic pulmonary tuberculosis:—LAENNEC, *Traité de l'auscultation médiate et des maladies des poumons et du cœur* II. Paris 1837; CARSWELL, *Pathological Anatomy* London 1838; RÜHLE, *Ziemssen's Cyclop.* V.; RINDFLEISCH, *Pathological Histology* II. London 1873; RAYMOND, *Arch. gén. de méd.* 1883; ORTH, *Virch. Arch.* vol. 86, *Berl. klin. Woch.* 1881; AUFRECHT, *Path. Mittheil.* I., II.; KÖSTER, *Sitzungsber. d. niederrhein. Gesell.* Bonn 1876; HUGUENIN, *Corresp. f. Schweizer Aerzte* 1880; ZIEGLER, *loc. cit.*; BUHL, *loc. cit.*; VON WYSS, *Gerhardt's Handb. d. Kinderkr.* III.; HAMILTON, *Pathology of bronchitis etc.* London 1883; CORNIL and RANVIER, *Man. Path. Hist.* II. London 1884; SORMANI, *Annal. univers. di med.* 1883; GERMAIN SÉE, *Bacillary phthisis* (trans. by WEDDELL) London 1885; ORTH, *Lehrb. d. spec. Path.* II. Berlin 1885.

References on tubercle-bacilli in sputum etc.:—KOCH, *Berl. klin. Woch.* 15, 1882 and 10, 1883; BAUMGARTEN, *Cent. f. med. Wiss.* 15, 1882; LICHTHEIM, *Fortschritte d. Med.* I. (1883); DE GIACOMI, *ibid.*; BALMER and FRAENTZEL, *Berl. klin. Woch.* 45, 1882 and *Deut. med. Woch.* 17, 1883; HILLER, *Deut. med. Woch.* 47, 1882, *Zeitschr. f. klin. Med.* V.; P. GUTTMANN, *Berl. klin. Woch.* 52, 1882;

PFEIFFER, *ibid.* 3, 1883; ZIEHL, *Deut. med. Woch.* 5, 1883; MENCHE, *Fortschritte d. Med.* I.; DRESCHFELD, *Brit. Med. Journ.* 1, 1883; DEMME, *Berl. klin. Woch.* 15, 1883; RIEGEL, *Cent. f. klin. Med.* 13, 1883; MÜLLER, *Verhandl. d. phys.-med. Gesell. zu Würzburg* XVIII. (1883), *London Med. Record* 1885; KOCH, *Mitth. a. d. k. Gesundh.* II. 1884; KLEIN and GIBBES, *Annual Report to Local Government Board* 1883–1884; PERCY KIDD, *Med. chir. Trans.* LXVIII. 1885; HUNTER MACKENZIE, *Treatise on the sputum* Edinburgh 1886; CORNIL and BABES, *Les bactéries* Paris 1885.

614. From what has been said in the last Article it will appear that the extension of localized tuberculosis of the lung is essentially a

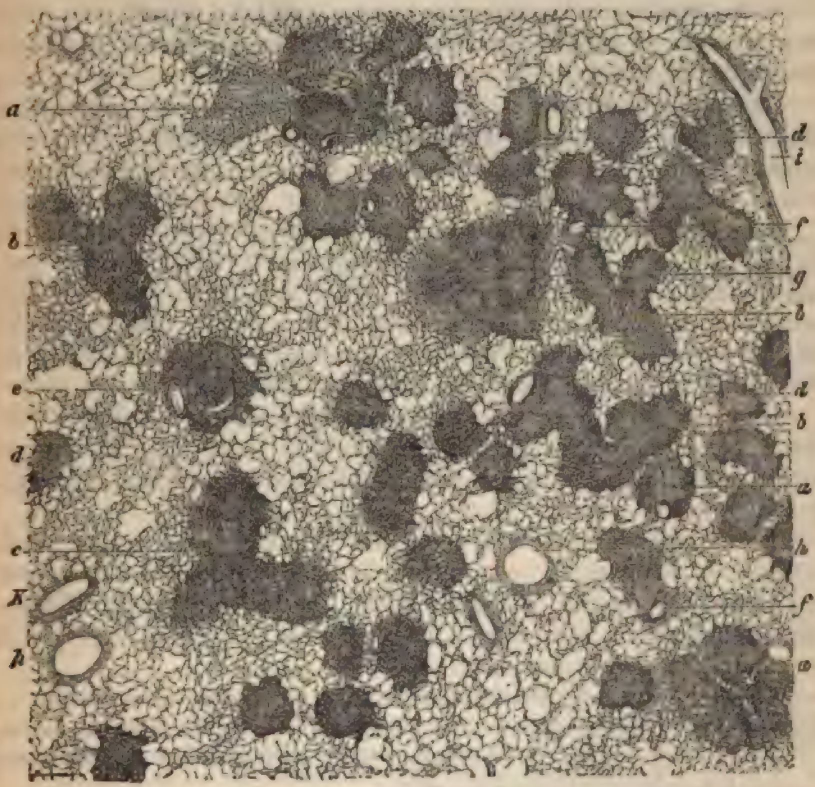

FIG. 238. CHRONIC NODULAR TUBERCULOUS BRONCHOPNEUMONIA.
(*Hardened in Müller's fluid, stained with picrocarmine* : × 6.)

a, b, c, d, nodules of various forms corresponding to systems of alveolar ducts
e, section through an infiltrated and occluded bronchiole
f, arteriole
g, nodules in process of coalescence
h, small bronchus (normal)
k, artery

bronchopneumonic process, accompanied to a varying extent by lymphangitis, bronchitis, and peribronchitis.

All these inflammatory processes affect in the first instance more or less isolated patches of tissue, which are usually nodular and vary from

the size of a millet-seed to that of a pea. Where the process is still recent we thus find the respiratory tissue studded with small gray translucent nodules, or larger white opaque ones (Fig. 238 *a d*). Most of these are simply respiratory bronchioles and alveolar ducts with their alveoli (*abcd*) which have become transformed by inflammation into compact and continuous masses. On section we can frequently make out in them the form and arrangement (*b c*) of the original parts. It is only when the nodule increases in size by the extension of the inflammation to neighboring alveolar groups and to the lymphatics that this configuration becomes indistinct and disappears.

In the later stages the bronchopneumonic nodules usually give place in a measure to those caused by lymphangitis, bronchitis, and peribronchitis (*e*); but this is by no means always the case.

Cases occur in which the thickening of the bronchi and peribronchial tissue and the occlusion of the smaller air-passages goes on to a very marked extent. In like manner the lymphangitis may spread far and wide.

If we start then with these nodular inflammatory patches it is not hard to gain an understanding of the many diverse forms in which pulmonary tuberculosis presents itself. They are all referable to this primary type, and their differences are due partly to varieties in the original bronchopneumonic patches themselves, partly to variations in the morbid phenomena which accompany their development.

As regards the bronchopneumonic patches, varieties occur chiefly in the character of the inflammatory exudation, to some extent also in the way in which the inflammation terminates—the issue of the inflammation.

In one case we may have a cellular or a fibrous exudation which rapidly becomes caseous or purulent, in another the process tends to fibrous overgrowth with partial caseation: thus we may distinguish caseous, caseo-purulent, caseo-fibroid, and fibroid or indurative varieties of tuberculous bronchopneumonia.

When the development of the nodular patches is accompanied by more extensive inflammation of the adjacent tissue, the nodular patch becomes a lobular one: thus we have a simply nodular and also a lobular form of tuberculous bronchopneumonia.

Both the primary and the secondary tuberculous patches may cease to extend and at length heal. It is very doubtful whether complete recovery of the affected tissue by re-absorption of the exudation is in any case possible, and indeed it can only occur in the very smallest patches whose vessels are not yet obliterated. In larger patches healing can only take place when the inflammatory process issues in fibrous hyperplasia and induration. The indurated portions of the lung are sometimes nodular, sometimes diffuse and extensive: they consist of slaty-gray (*induration ardoise*) or white fibrous tissue. They may contain

caseous residues; but usually some exist scattered through the tissue, and are derived either from bronchopneumonic patches or from altered bronchial secretion. In these nodules and patches it appears likely that bacilli may persist for a considerable time, though we may take it for granted that they ultimately perish. Sooner or later the caseous residues become calcified.

In this way, so long as the affected patches are few, tuberculous disease of the lung may be entirely recovered from, or at least stayed from further advance, so that for years no new portion of the lung is invaded. Of course so long as any bacilli remain in the tissue, we can hardly speak of the recovery as complete. When a large number of tuberculous foci exist in the lung, in some of them absolute or relative recovery may take place, but it is extremely unlikely that this will occur in all simultaneously. So long however as a single patch undergoes disintegration and forms a nidus for the multiplication of the bacilli, the danger and the probability remain that the process may start afresh by extension through the lymphatics, the blood-vessels, or the air-passages.

The term tuberculous bronchopneumonia (including the associated morbid changes) is to a great extent coextensive with the clinical term **pulmonary phthisis.** The two ideas are however not identical. The lung may be destroyed by inflammations which have nothing to do either with tuberculosis or with any other of the infective granulomata. Inasmuch as phthisis primarily connotes simply destruction of tissue, it might very well be taken to include all destructive inflammations of the lung.

It is usual however to limit the term to those destructive inflammations which are progressive, that is to say which advance either steadily or intermittently from bad to worse, and that independently of fresh injury from without. This limitation then excludes those affections of the lung wherein an acute inflammation is followed by a partial destruction of tissue, which however has no tendency to extend or become general.

Even then the terms phthisis and tuberculosis are not equivalent. For as we have seen certain non-specific inflammations may take on a progressive character, and of the specific granulomatous infections glanders, syphilis, and actinomycosis lead to affections of the lung analogous to tuberculous disease.

The varieties observed in the course of tuberculous bronchopneumonia, in other words the diversities in the nature of the individual foci of inflammation, depend partly on differences in the reaction of the pulmonary tissue to irritation in different persons, but chiefly no doubt on the character and quantity of the irritant disseminated through the lung. And though our view at present is that the essential and specific irritant in tuberculous phthisis is the tubercle-bacillus, yet it can hardly be gainsaid that in many cases other injurious agencies cooperate with it.

Many pulmonary cavities or vomicæ contain not only tubercle-bacilli but also other bacilli and micrococci, and these too may have a destructive action, modifying and perhaps now and then intensifying the action of the specific virus. It is possible that the caseo-purulent form of phthisis may be due to a complex infection of this nature.

With regard to recovery from pulmonary tuberculosis, many cases have been recorded; but until the discovery of the tubercle-bacillus it was impossible to de-

cide with absolute certainty whether when a cicatrix was found in the lung the antecedent affection had or had not been tuberculous. The process of healing referred to in the text undoubtedly occurs: we would refer in support of this not only to cases in which a clinical diagnosis of tuberculosis had been made, and years afterwards the indurative changes above described have been discovered in the lung, but also to a recently-published observation of NAUWERCK'S (*Deut. med. Woch.* 23, 1883). In the body of a man of 45, who five years before his death had for a time shown symptoms of bilateral disease of the apices of the lungs, and who died after a short illness of gastric cancer, NAUWERCK found in the apices cicatricial patches enclosing scattered caseous foci with a few tubercle-bacilli. There was no trace of recent tuberculous bronchopneumonia or lymphangitis. In the indurated fibrous tissue no bacilli were found. It is worth noting that four brothers of the patient had previously died of tuberculosis.

615. The simplest and commonest form of pulmonary tuberculosis is **nodular tuberculous bronchopneumonia,** characterized by the formation of bronchopneumonic nodules and nodes.

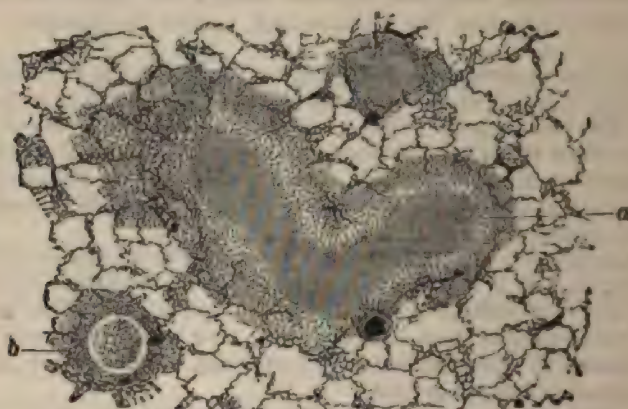

FIG. 239. NODULAR TUBERCULOUS BRONCHOPNEUMONIA.

(Preparation injected with blue, and stained with carmine: × 25.)

a, v-shaped patch, caseous in the centre and fibro-cellular at the periphery, produced by the infiltration of two contiguous alveolar ducts and their alveoli
b, respiratory bronchiole with cellular exudation in and around it
c, alveolar duct, with caseous cellular contents and infiltrated alveoli

To give rise to it there must somewhere exist a mass of softening tubercle, a tuberculous bronchitis, or a bronchiectatic cavity: in other words a focus from which tubercle-bacilli may reach the bronchial passages and thence pass into the terminal bronchioles (Fig. 239 *b*).

If the dissemination is rapid and extend over the greater part of the lung the patient may sink very speedily, and after death the lung is found studded with miliary gray and white nodules exactly resembling embolic tubercles. This form we might describe as miliary tuberculous bronchopneumonia (Fig 237). The small patches lie partly in the alveolar ducts (Fig. 239 *c*), partly in the respiratory bronchioles (*b*): when

recent they are cellular, but afterwards they become caseous or fibrous. The vessels perish as the nodules develop.

When the virus is more gradually disseminated, so that the patient survives for a longer time, the patches become more numerous and increase in size. As a rule they become caseous in the centre (*a*) and fibrous or fibro-cellular at the periphery. The course of the disease is usually chronic, and it might therefore be described as **chronic nodular indurative bronchopneumonia.** The groups of gray or grayish-white nodules are arranged in clusters, and in section appear rounded, oval, bifurcated, or trifoliate. This is of course due to the fact that the solid nodular masses represent the terminal branches of a respiratory bronchiole. In the neighborhood of the nodules there are always a number of obstructed bronchioles with thickened walls, looking on section like encapsuled caseous nodes.

At first the bronchopneumonic patches lie bedded in normal air-containing tissue; but after a time the surrounding tissue is usually condensed, indurated, and gray. This is due in the first place to collapse from occlusion of the bronchioles and small bronchi, and secondly to extension from the nodular patches of the inflammatory infiltration and induration, by which the alveolar walls are thickened and the alveoli are filled up with cells and ultimately fibrous tissue. The pigmentation is referable partly to inhaled dust, partly to the small hæmorrhages which occur from disturbances of circulation in the diseased area or from rupture of the degenerate vessels that run through it.

The rarer form of nodular tuberculosis, **nodular caseous bronchopneumonia,** is characterized by the formation of small cellular foci, gray or yellowish-white, and rapidly becoming caseous or purulent. The caseous non-vascular nodules are always surrounded by a zone within which the alveoli are filled with leucocytes, desquamated epithelium, liquid exudation, and often fibrin, while the lung-tissue itself is infiltrated with small cells. These nodules readily soften and break down, so that little cavities are formed which sooner or later open into the adjacent bronchi.

The caseous, indurative, and caseo-fibroid forms of bronchopneumonia are met with in combination.

616. The processes just described start as a rule in the **apices of the lungs,** and thence extend downwards and backwards. The apex of a lung may thus exhibit terminal stages of the disease while the bases are still in process of invasion. After a time the parts most affected, in the caseo-fibroid or indurative form of bronchopneumonia, become almost absolutely airless, and hard and knotty to the touch. The pulmonary pleura is usually much thickened and adherent to the costal layer (Fig. 240 *a*), the lung-tissue is condensed and studded with caseous nodes (*bc*) surrounded either by translucent gray or white or by slaty-gray pigmented fibrous tissue. These nodules are occluded and indurated alve-

olar ducts with their alveoli (*b*), or bronchioles with caseous contents (*c*) and thickened walls surrounded by condensed tissue. Between the nodules lie white or pigmented fibrous bands (*e*) corresponding to thickened interlobular septa or peribronchial connective tissue, and gray nodules representing recent foci of inflammatory infiltration (ff_1).

The fibrous nodes and bands are coarsely-fibrous with few cells, or mainly cellular. Some of the nodes are caseous in the centre, giant cells being often found in the zone between the caseous matter and the non-necrosed tissue. By appropriate treatment a few scattered bacilli can be demonstrated. Sometimes these indurated patches also contain typical tubercles. The septa of the remaining portions of the lung are frequently infiltrated with cells and more or less thickened.

This morbid change may extend over the greater part of the lung,

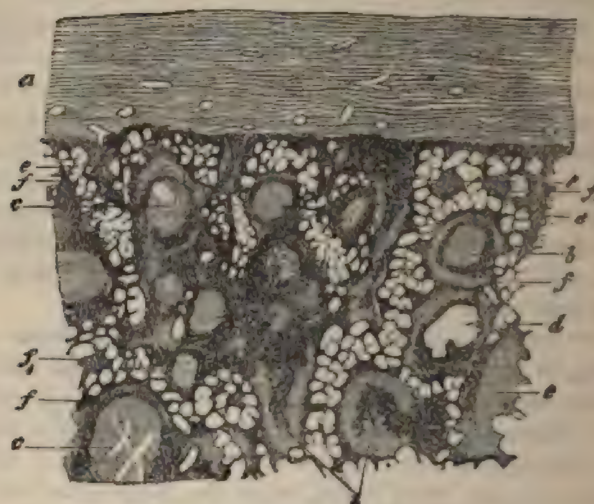

FIG. 240. CHRONIC NODOSE TUBERCULOUS CIRRHOSIS.

(*Hardened in alcohol, stained with hæmatoxylin*: × 30.)

a, thickened and fibroid pleura
b, caseo-fibrous bronchopneumonic nodes
c, bronchioles with caseous contents and thickened walls
d, small bronchiectatic cavities
e, thickened interlobular septa
f, recent cellular infiltration surrounding the nodules and (f_1) the lymphatics.

The alveolar septa are in parts infiltrated with cells, and the thickened and indurated tissue is pigmented.

and then leads to a form of contraction and induration which we may fitly describe as **nodose tuberculous cirrhosis.** Usually however it is confined to a limited portion of the lung, other changes being set up which lead to a different result.

Even in cases where the cirrhosis is at first the characteristic feature ulceration is never entirely absent. The process may start in the caseous foci within the lung-tissue itself, or in the bronchiectatic cavities

which arise in the shrunken and airless parts. Once the process of disintegration has begun it usually advances steadily and somewhat rapidly to the formation of vomicæ or caverns. Even when these cavities become lined with a layer of granulations the process is seldom thereby brought to a complete standstill, for the bacilli settled in the wall of the cavity give rise to fresh inflammatory change and fresh necrosis.

The usual course of the disease, in indurative tuberculous bronchopneumonia as in other forms, leads to the formation of cavities of considerable size, increasing not only by continuous extension but also by coalescence with others. In the latter case we may have a whole series of intercommunicating cavities, or a single large and very irregular cavern traversed and partially subdivided by bands and fragments of tissue.

The greater part or the whole of the upper lobe and parts of the lower lobe may be thus destroyed, the cavity being in places bounded only by the thickened pleura, while the collapsed and indurated pulmonary tissue is much reduced in bulk. The cavity contains air, and grayish, yellowish, or brownish liquid, mingled with pus-cells and whitish shreds and fragments of necrotic lung-tissue usually beset with bacilli. The disintegration of the lung-tissue takes place much more rapidly in caseous and caseo-purulent bronchopneumonia than in the indurative form. It sometimes happens that in a very short time from the onset of the malady the whole lung is riddled with cavities, whose caseous and infiltrated walls break down into shreds as if they were rotten. When such a cavity lies immediately underneath the pleura there is always (unless previous adhesions limit the process) a certain amount of fibrinous or purulent inflammation of that membrane. Not infrequently the pleura is perforated and **pneumothorax** or **pyopneumothorax** is set up.

The caseo-fibroid, caseous, and caseo-purulent forms of bronchopneumonia occur in various combinations and give rise to a great variety of different morbid appearances in different cases. Sometimes a suppurative form of the inflammation is grafted on a chronic caseo-fibroid form, and leads to a marked acceleration of the destructive process.

The striking fact that tuberculous bronchopneumonia usually begins in the apex of the lung points to the conclusion that the settlement and multiplication of the tubercle-bacilli take place more readily there than in other parts. In the apex the respiratory movement is relatively smaller, and the amount of blood in circulation less. Any bacilli which may reach the apex by aspiration are therefore less readily carried off by the lymphatics and destroyed by the living tissue-cells: in other words the tissue is there less resistant. A fact perhaps still more significant is this—that residues of previous inflammation (Art. 611) linger longer in the apex than elsewhere in the lung, and in this way cause a kind of local weakness or predisposition to bacillary invasion in that part.

617. **Lobular caseous tuberculous bronchopneumonia** always

starts in miliary or nodose bronchopneumonia. Sometimes in the neighborhood of recent cellular or partially caseous bronchopneumonic foci (Fig. 241 *a*) a lobular inflammation is set up, which is marked by cellular infiltration of the alveolar (*b*) and interlobular (*c*) septa, and distention of the alveoli and lymphatics (*d*) with a fibrinous liquid and cells. The tissue thus infiltrated sooner or later becomes caseous and breaks down, induration seldom occurring to any appreciable extent.

At first the inflamed lobules appear on section airless, grayish-red, smooth, gelatinous, and infiltrated: the condition has been well described as **gelatinous infiltration.** They afterwards become paler, then gray and translucent, and lastly opaque yellowish-white.

The number of the lobules so affected is of course variable. When they are numerous we usually find at the time of death that different

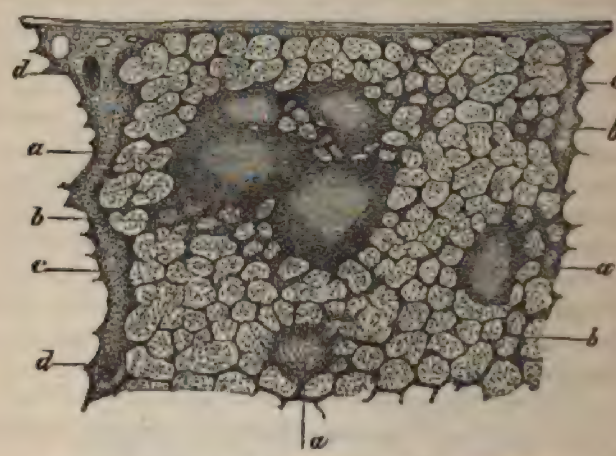

FIG. 241. LOBULAR CASEOUS TUBERCULOUS BRONCHOPNEUMONIA.

(*Section through a subpleural lobule; hardened in alcohol, stained with hæmatoxylin.* × 25.)

a, nodule with caseous centre and cellular pheripery
b, alveoli filled with exudation, the walls infiltrated with leucocytes
c, interlobular septa infiltrated with leucocytes
d, lymphatics filled with exudation

lobules are in different stages of the process, some being grayish-red, others gray, others yellowish-white. Frequently the latter show signs of softening and excavation, or there are actually cavities of considerable size and communicating with the air by way of the bronchi.

When all the lobules of a lobe are thus affected, the disease assumes the appearance of a lobar affection and is often so described (Art. 606). Microscopical examination however always proves that some of the lobules have been affected long before the others, and so does away with the idea of a 'lobar caseous pneumonia.'

The pleura over the affected lobules is always inflamed, and usually

covered with fibrinous exudation. As the lobules break down the pleura may suppurate and become caseous, and so break down in like manner.

When lobular caseous bronchopneumonia is found in a lung we always find also older morbid changes in it, usually at the apex but at times in other parts. They may be slight, consisting of a few scattered points of caseation, or some indurated nodules, or dilated bronchi. In other cases the lobular caseation is but a terminal complication of an advanced nodose, caseous, or indurative bronchopneumonia. The lobular process may in fact be combined in a multitude of ways with the nodose.

Lobular caseous bronchopneumonia is most frequent in children, though it is by no means rare in adults. By many pathologists it is referred to as **scrofulous pneumonia**.

618. **Bronchopneumonia from actinomycosis, glanders, and syphilis.** The pulmonary affection set up by *Actinomyces* (Art. 134) takes the form of a bronchopneumonia, the diseased patches being of miliary size or larger. In cattle the patches are hard and nodular, and contain in the centre the ray-fungus as a kind of nucleus (PFLUG, HINK). In man the affection tends to be suppurative (ISRAEL, PONFICK), yellow or grayish-yellow patches being formed which presently by softening and suppuration give rise to corresponding cavities. These may become larger and larger, and at length break through the pleura. The characteristic feature of the process is of course the presence of the ray-fungus in the pus and in the infiltrated and disintegrated lung-tissue.

When glanders-bacilli (LÖFFLER and SCHUTZ, *Deut. med. Woch.* 52, 1882; CORNIL and BABES, *Les bactéries* Paris 1885) reach the lung by aspiration, they give rise to the formation of nodules and nodes chiefly beneath the pleura. At first they are soft and grayish, afterwards they become firmer and in part caseous. Patches of lobular extent and grayish-red in tint, and patches of bronchopneumonic suppuration, are also met with in glanders, and there may be a certain amount of hæmorrhagic inflammation. When the disease affects a number of contiguous lobules, large portions of the lung may in this way be infiltrated and ultimately break down. When the bacilli reach the lung through the circulation they induce pneumonia, which resembles in many respects the bronchopneumonic forms just referred to.

Syphilis first of all gives rise to bronchitis, which in course of time leads to peribronchial induration, with occlusion and dilatation of bronchi (Arts. 578–579). According to some catarrhal, indurative, suppurative, and caseous forms of bronchopneumonia may also result from syphilis. The caseous forms are said to include both lobular and nodular varieties.

References on pulmonary actinomycosis:—ISRAEL, *Virch. Arch.* vols. 74, 78, and *Beitr. z. Kenntn. d. Actin. d. Menschen* Berlin 1885; PONFICK, *Die Actinomycose des Menschen* Berlin 1882; PFLUG, *Cent. f. med. Wiss.* 14, 1882; HINK, *ibid.* 46, 1882; MARCHAND, Article *Aktinomykose*, *Eulenburg's Real-encyclop.*

On pulmonary glanders see BOLLINGER, *Zeitschr. f. Thiermed.* 1876, Ziemssen's

Cyclop. III.; WERNER, *Der Lungenrotz* 1878; RABE, *Jahresber. d. Thierarznei-schule* Hanover 1876; PÜTZ, *Seuchen u. Herdekrankheiten* Stuttgart 1882; DIECKERHOFF, *Lehrb. d. spec. Path. f. Thierärzte* I. Berlin 1885.

On pulmonary syphilis see Art. 518.

CHAPTER LXXXVIII.

TUMORS AND PARASITES OF THE LUNGS.

619. **Primary tumors** of the lung or bronchi are rare. Primary **carcinoma** may occur in the larger bronchi as irregular nodose or papillary growths, starting either in the mucous glands or in the lining epithelium. Similar growths are also met with in the smaller bronchi, and these tend to spread over large portions of the bronchial ramifications. The disease may then extend to the peribronchial lymphatics, whereupon its generalization takes place with great rapidity, the air-passages both of the part originally affected and of remoter parts becoming studded with white marrowy nodes and nodules. The disease ultimately attacks the interlobular lymphatics and the lymphatic glands. In a third form of carcinoma large solitary nodes appear, of which we cannot say whether they start in the bronchioles or in the alveoli. They enlarge by the continual invasion and filling up of the alveoli at their borders with the cancerous epithelial growth. They also may invade the lymphatics and then extend in the same way as the second form. CHIARI has described a nodular **adenoma** of the mucous glands in the bronchial mucous membrane.

ROKITANSKY, MORGAN, RINDFLEISCH, and others have described cases of **fibroma,** in which nodules from the size of a hemp-seed to that of a hazel-nut were formed in large numbers around the bronchi. **Osteoma** also occurs in the form of irregularly-shaped structures with jagged processes, and of rounded nodules of the size of a pea; small globular chondrolipomata (ROKITANSKY, CHIARI), and **enchondromata** starting from the bronchial cartilages, have also been met with.

Of **secondary growths** examples of each kind that forms metastases at all have been found in the lungs. When the tumor-cells reach the lung as emboli they usually produce rounded nodules having the characters of the parent-tumor. These start from the embolized blood-vessels, and grow by radial extension or concentric accretion, partly invading and partly compressing the pulmonary tissue. The lymphatics may likewise be invaded by the growth, which then advances by this channel. When the tumor-cells originally reach the lung or pleura by the lymphatics, nodules of various sizes appear along the course of the latter. In the case of cancer the diffusion is often remarkably uniform, so that the lymphatics of a large portion or the whole of the lung are

distended with white marrow-like masses. On section such a lung exhibits a number of close-set whitish or reddish nodes along the course of the bronchi or interlobular septa.

The neoplastic growth often sets up inflammations especially of the pleura, and these not infrequently are hæmorrhagic in character.

Primary carcinoma of the lung:—ROKITANSKY, *Path. Anat.* IV.; EBERTH, *Virch. Arch.* vol. 49; LANGHANS, *ibid.* vol. 53; PERLS, *ibid.* vol. 56; WEICHSELBAUM, *ibid.* vol. 85; SCHOTTELIUS, *Ein Fall v. prim. Lungenkrebs* In. Diss. Würzburg 1875; FENLEY and PARKER, *Med. chir. Trans.* LX. (1877); STILLING, *Virch. Arch.* vol. 83; REINHARDT, *Arch. d. Heilk.* IX. (1878); CHIARI, *Prag. med. Woch.* 1883; BECK, *Zeitschr. f. Heilk.* V. 1884.

Connective-tissue tumors of the lung:—ROKITANSKY, *Path. Anat.* IV.; MORGAN, *Trans. Path. Soc.* 1871; VIRCHOW, *Krankh. Geschwülste* II.; FÖRSTER, *Virch. Arch.* vol. 13; RINDFLEISCH, *ibid.* vol. 81; HESSE and E. WAGNER, *Arch. d. Heilk.* XIX.; HÄRTING and HESSE, *Eulenburg's Vierteljahrsschr.* XXX., XXXI.; CHIARI, *loc. cit.*; RIBBERT, *Virch. Arch.* vol. 102 (lymphoma); COHN, *ibid.* vol. 101 (osteoma).

HESSE and WAGNER state that the Schneeberg miners frequently suffer from peculiar tumors in the lung, which WAGNER describes as lymphosarcomata. COHNHEIM (*Allgem. Pathol.* I.) suspects that they are due to some form of infective granuloma.

620. The **animal parasites** infesting the bronchi and the lungs are not numerous. The most important is *Echinococcus*, which may form hydatid cysts of considerable size, with or without daughter-cysts. *Cysticercus cellulosæ* is rare. *Strongylus longevaginatus*, a cylindrical worm 15-26 mm. long, has once been found in a boy's lung, and ORTH discovered a calcified *Pentastoma denticulatum* (Art. 225). KANNENBERG has in several cases of gangrene of the lung discovered *Monas lens* and *Cercomonas* (Art. 250), two flagellate infusorians, among the shreds of lung-tissue in the sputa. In the resting state they look not unlike white blood-corpuscles.

Of **vegetable parasites** in the lungs the most noteworthy are the numerous varieties of bacteria. Some of these, such as the bacilli of tuberculosis and of glanders, and the micrococcus of pneumonia, give rise to specific inflammations. Others again, such as those which inhabit the mouth, may possibly give rise to non-specific inflammations of various intensity when aspirated into the air-passages.

Gangrenous portions of the lung contain micrococci, bacilli, and spirilla. Some of these have probably much to do with the gangrenous decomposition, others probably settle only in the already disintegrated tissue.

In tuberculous cavities, disintegrating hæmorrhagic patches, croupous exudations within the bronchi and trachea, etc. we occasionally meet with a micrococcus which subdivides like *Sarcina* into tetrads, and has accordingly been regarded as a minute variety of that species (HEIMER). It usually occurs at the same time also in the pharynx and larynx, and has probably no causal connection with the respective diseases in ques-

tion. It is however not impossible that it may have the power of setting up inflammation where it settles.

Of the filamentous fungi or hyphomycetes we find in the lung the bovine *Actinomyces*, and various forms of *Aspergillus* and *Mucor*. The former is the only one that possesses any great pathological importance: the others, with *Oïdum*, settle only in decomposing lung-tissue, stagnating secretions, or hæmorrhagic infiltrations. The above-named mould-fungi now and then proceed to the stage of fructification within the lung.

References on fungi in the lung or **pneumonomycosis**:—VIRCHOW, *Froriep's Notizen* 1846, *Virch. Arch.* vols. 9, 10; FRIEDREICH, *ibid.* vol. 30; COHNHEIM, *ibid.* vol. 33; BRISTOWE, *Trans. Path. Soc.* 1854; MUNK, *Cent. f. med. Wiss.* 1864; HEIMER, *Ueber Pneumonomycosis sarcinica* In. Diss. Munich 1877; NAUWERCK, *Corresp. f. Schweiz. Aerzte* XI. (1881); FRIEDREICH, VON DUSCH, and PAGENSTECHER, *Virch. Arch.* vols. 10, 11; P. FÜRBRINGER, *ibid.* vol. 66; ROSENSTEIN, *Berl. klin. Woch.* 1867; LICHTHEIM, *ibid.* 1882; BOLLINGER, *Zur Aetiol. d. Infectionskrankheiten* Munich 1881; AUFRECHT, *Path. Mittheil.* II. 1883; KANNENBERG, *Virch. Arch.* vol. 75, *Zeitschr. f. klin. Med.* I. 1880.

According to BAELZ (*Cent. f. med. Wiss.* 39, 1880) a peculiar parasitic disease of the lung (*gregarinosis pulmonum*) is very common in Japan. Patients affected with it spit blood for a number of years, and their lungs contain encysted brownish-yellow ovoid *Psorospermia* and clear or pale-yellow non-encysted granular round or ovoid *Coccidia* (Art. 250). The affection is also met with in Formosa, and according to MANSON is due to the presence in the lung of *Distoma ringeri*, of which BAELZ'S *Psorospermia* are said to be merely the ova (*Med. Times and Gaz.* 2, 1881, and 2, 1882, *Brit. Med. Journ.* 2, 1882).

CHAPTER LXXXIX.

THE THYROID GLAND.

621. The **thyroid gland** is developed from a vesicular diverticulum of the throat-cavity, which afterwards becomes detached; its epithelium proliferates and grows into the surrounding fibrous tissue as cords and masses of cells, which form the primitive gland-tubes and follicles. Cavernous blood-vessels penetrate among these cell-masses and divide up the rudimentary gland into groups of cells of various sizes. These vessels are then differentiated into arteries, capillaries, and veins of ordinary dimensions, in the meshes of which the mature glandular structures make their appearance. These consist of rounded masses and cords of cells, forming follicles which at or soon after birth exhibit a central lumen distended with secretion or containing a little granular detritus. The cells surrounding the lumen are cubical or cylindrical and are seated directly on the blood-vessels. Between the follicles lie a number of what we may call unutilized epithelial cells; in the later stages of growth these may be fashioned into new follicles. Papillary overgrowth of the epithelium may also lead to the subdivision of an old follicle into two or more new ones.

In the fully-developed gland we can distinguish a cortical and a medullary substance: the latter contains radially disposed follicles and gland-tubes, the former masses and cords of cells concentrically arranged. In later life some of the glandular follicles contain colloid matter (Fig. 242 *c*).

In old age the substance of the gland undergoes more or less marked atrophy, the follicles shrinking to clusters of small cells or disappearing altogether, and the fibrous stroma becoming homogeneous and indurated, and at the same time increased in relative amount.

The adult thyroid consists of two lateral lobes and an isthmus uniting the two across the front of the trachea. The vertical diameter of a lateral lobe is 5–7 cm., the breadth 3–4 cm.; the width of the isthmus varies from 4 to 20 mm. Very frequently there is a middle lobe or pyramid, which rises from the isthmus and grows upward.

Absence of the thyroid is rare. More common **anomalies** are—abnormal smallness or absence of a lobe or of the isthmus, abnormal largeness, multiple lobes, and accessory glandular masses separate from the main mass and connected with the hyoid, the deeper parts of the

trachea, the supraclavicular fossæ, the interior of the larynx (P. BRUNS), the aorta, or the posterior wall of the pharynx. In very rare instances the isthmus is found to pass between the trachea and the œsophagus.

The most important of the morbid changes to which the thyroid is liable are those forms of enlargement of the whole gland or of particular parts of it included under the general term **goitre,** bronchocele or thyreocele (*struma*).

The gland may be enlarged from birth and constitute a **congenital goitre.** The enlargement may be due to over-distention or telangiectatic dilatation of the vessels, to hypertrophy of the gland-tissue, to premature and excessive colloid deposit, to increase of the fibrous stroma, or to adenomatous growth. The hyperæmic enlargement is of course transient, but the other varieties persist.

vessels gland tis Colloid fibrous Adenom

In later life also the thyroid may be enlarged by hyperæmic distention, constituting **vascular goitre.** The condition is not usually lasting, though it may become chronic.

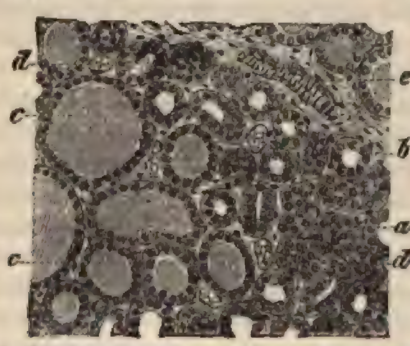

FIG. 242. GOITRE PARTLY HYPERTROPHIC AND PARTLY COLLOID.

(*Alum-hæmatoxylin staining:* × 60.)

a, follicles filled with cells
b, empty follicle
c, colloid masses
d, capillaries
e, stroma with arteriole

A second form named **hypertrophic goitre** is due to multiplication and enlargement of the normal cell-masses (Fig. 242 *a*) and follicles (*b*), or to increase of the normal colloid contents (*c*). In the first case we have parenchymatous or follicular or **granular** goitre, in the second case colloid or **gelatinous** goitre.

The new follicles arise (WÖLFLER) from unutilized glandular cells, either by direct multiplication and grouping into orderly masses, or by endogenous multiplication of individual cells. The new follicles are separated from each other by fibrous tissue and blood-vessels. Pure hypertrophy of the thyroid is however not very common. It may be general or localized, and may exist from birth.

Adenoma of the thyroid is an epithelial new growth occurring in the form of isolated nodules, or diffused over one or both lobes. It consists

of vascular non-typical gland-like tissue, which persists in this form or is transformed more into the likeness of the normal gland-tissue. WÖLFLER distinguishes four varieties—the fœtal, the gelatinous, the myxomatous, and the columnar-celled. These adenomata occasionally recur after excision, and are not easily distinguished from carcinomata.

Fœtal adenoma arises from some rudiment of embryonic tissue, though its growth may not be apparent till puberty or pregnancy: it occurs in nodes from the size of a pin's head to that of the fist. Its tint is pale-yellow, dark-red, or brownish-black, according as it is less or more vascular.

The nodes grow in much the same way as the gland originally develops; the smallest nodules accordingly consist of proliferous masses of round or oval not very sharply-defined cells, interspersed with dilated and varicose vessels. By degrees these vessels are differentiated into narrow capillaries and wider trunks, and then again assume gradually the typical configuration of the vascular system of the gland, while the proliferous epithelial cells become arranged in groups and follicles.

The nodes do not however reach this degree of development, but remain in various intermediate stages.

Adenomata, both small and large, which are traversed by numerous cavernous vessels, and so have a dark-red tint, are very liable to internal hæmorrhages. The glandular follicles within an area of extravasation not infrequently dilate into ramifying channels, which by and by are constricted off into vesicular cavities. Large extravasations are sometimes transformed into hyaline masses which afterwards becomes vascularized and traversed by bands and cords of proliferous glandular cells. In other instances scar-like or homogeneous cicatricial tissue is formed, and contains here and there dilated blood-vessels.

Gelatinous adenoma is a tumor, nodulated, tuberous, or smooth, occupying the whole gland or a single lobe, and on section appearing of a fairly uniform jelly-like consistence. The scanty stroma of the gland is in fact pervaded and distended by variously-sized lumps of colloid substance.

The growth starts in the granular cells which lie between the true follicles. As these cells multiply they give rise to new follicles or acini which secrete the colloid matter. These growths indeed are related on the one hand to the simple hypertrophies, on the other to medullary carcinoma. WÖLFLER distinguishes two varieties of gelatinous adenoma—interacinous adenoma, and cyst-adenoma. **Interacinous** adenoma, as it may briefly be called, is the commonest form of goitre and the largest. It consists essentially of gland-like vesicles or cysts filled with colloid substance and lined with cubical or spherical epithelial cells. Between the fully-formed vesicles lie rudimental cell-masses and follicles in process of development. The epithelial cells of the older vesicles may multiply to such an extent as to fill them up (*adenoma interacinosum*

proliferans). Interacinous adenoma may co-exist with the fœtal form. **Cystadenoma** is characterized by the formation of cysts varying in size from that of a lentil to that of a goose's egg. The proliferous cells which these cysts contain undergo fatty and colloid degeneration. The intercystic vessels and fibrous tissue become atrophied. In some parts the interacinous cell-groups grow and break into the cysts, and there undergo colloid change: or they may simply push the cyst-epithelium before them, and the papillary ingrowths thus formed tend to become covered with cylindrical cells. New cysts are sometimes formed in the substance of these ingrowths, and thus the original cysts may become filled with minor cysts. Nodes containing cysts and ingrowths of this kind are described as proliferous cystadenomata, and occasionally lead to the formation of enormous goitres in which the whole of the thyroid is included. In the human subject however they are not common: in the monkey and the dog these formations occur in the normal gland. The neoplasm is usually most characteristically developed in the central parts of the goitre; the periphery consists mainly of non-excavated follicles and cell-masses. The intercystic stroma is frequently fibromyxomatous, or consists of hyaline tissue resulting from hæmorrhagic infiltration. The colloid substance is formed only in small quantity by the cylindrical epithelium of the papillary ingrowths. Sometimes the glandular follicles and vesicles become calcified, their epithelium undergoing fatty degeneration.

Myxomatous adenoma (follicular and tubular) occurs both in young and in old patients: it takes the form of soft nodose growths of various sizes and often highly vascular. The neoplasm consists of a hyaline structureless or faintly striated matrix, occasionally in part calcified, interspersed with solid globular cell-masses, follicles, and cords of cells of various forms. Normal follicles are as a rule conspicuously absent.

The myxomatous condition is secondary, being a transformation of a fœtal or interacinous adenoma. The transformation is due to hæmorrhagic infiltrations of the tumor-tissue such as are known to occur at puberty, during the catamenia, and during pregnancy. The infiltrated area assumes a hyaline appearance, or if it is partially vascularized it becomes more fibrous and ultimately fatty and calcareous: if the vascularization is more complete the glandular cells multiply and the growth is pervaded with new-formed cell-masses and tubules.

Columnar-celled adenoma is characterized by the presence in it of vesicles or acini lined with tall columnar epithelium, and traversed by irregular solid cords and bands made up of the same kind of cells. The new growth is distinguished from mere hypertrophy of the follicles that are lined with columnar epithelium in the normal gland by the presence of glandular tubules of the embryonic type. According to Wölfler this form is very rare.

Goitre is dangerous to the patient afflicted with it chiefly from

the pressure it may exert on the trachea, the œsophagus, or the large vessels of the neck. The trachea is compressed when the goitre grows down beneath the sternum, or when it reaches a very large size and surrounds the trachea and œsophagus or pushes them to one side. The continuous pressure sometimes causes atrophy of the tracheal cartilages, and the tumor then protrudes into the air-passage. Accessory thyroid glands may become goitrous like the principal mass.

References :—ECKER, *Zeitschr. f. rat. med.* VI. 1847; LEBERT, *Die Krankh. d. Schilddrüse* Breslau 1862; FRIEDREICH, *Virchow's Handb. d. spec. Path.* V. 18[illegible]; ROKITANSKY, *Anat. d. Kropfes* Vienna 1849; DAVIES, *Trans. Path. Soc.* 1849; VIRCHOW, *Krankh. Geschwülste* III.; LÜCKE, *Pitha u. Billroth's Handb. d. Chir.* III. 1875; DEMME, *Gerhardt's Handb. d. Kinderkr.* III.; STROMEYER, *Arch. f. phys. Heilk.* IX. (1850) GUILLOT, *Arch. générales* 1860; PARSONS, *Med. Times and Gaz.* 2. 1862; KÖNIG, *Arch. f. Heilk.* 1865; GEUZMER, *Virch. Arch.* vol. 74; LÜCKE, *D. Zeitschr. f. Chir.* VII.; KAUFMANN, *ibid.* XVIII.; W. MÜLLER, *Jena. Zeitschr. f. Med.* VI. 1871; COHNHEIM, *Virch. Arch.* vol. 68; BUOB, *Du goître congén.* Strasburg 1867; HECKER, *Monatsschr. f. Geburtskunde* XXXI. 1868; SPIEGELBERG, *Würzburg. med. Zeitschr.* 1864; NIÈPCE, *Traité du goître* Paris 1851; LUTON, Art. *Goître. Nouv. dict. de méd.* XVI. 1872; BERGER, *Arch. de méd.* 1874; HILDEBRAND, Art. *Struma, Eulenburg's Real-encyclop.*; WÖLFLER, *Ueb. d. Entwickelung u. d. Bau d. Schilddrüse* Vienna 1880 and *Entwick. und Bau d. Kropfes, Langenbeck's Arch.* XXIX. 1883; MADELUNG (accessory thyroids) *ibid.* XXIV.; LEITZ, *ibid.* XXIX.; GORE, *Fortschr. d. Med.* I. 1883; GUTKNECHT, *Virch. Arch.* vol. 99; STRECKEISEN, *ibid.* vol. 103.

The account in the text is based chiefly on the recent admirable researches of WÖLFLER: without agreeing with him in all details we think his work the best that has yet appeared on the structure and genesis of goitre.

622. The adenomata described in the last Article do not in general extend beyond the limits of the thyroid gland, and are therefore to be classed with the innocent or non-malignant growths. Varieties of proliferous cystadenoma and follicular adenoma do however occur, which are characterized by their vascularity, their highly cellular nature, and their rapid growth; and these are apt to recur after excision. Other varieties depart more or less from the adenomatous type, approaching that of carcinoma, and these may form metastases.

These transitional varieties are best described as **malignant adenomata** (WÖLFLER). They have in parts a grayish-white medullary or encephaloid appearance, and contain amid structures unmistakably adenomatous patches exactly resembling carcinomatous tissue. This is the case even when the metastatic growths have a structure almost exactly corresponding to that of the normal thyroid gland. In considering the statement of COHNHEIM and HESCHL—that normal thyroid hypertrophies and apparently innocent adenomata may give rise to metastases—we must therefore bear in mind also that malignant adenoma and carcinoma are occasionally accompanied by metastatic growths whose structure closely resembles that of non-malignant adenomatous tissue.

Even in the parent-tumor in the latter case we at times find structures very similar to normal thyroid acini with a lumen and a regular epithelial lining.

Carcinoma of the thyroid occurs in regions where goitre is endemic, and usually develops in an existing goitrous growth. As a rule it is soft and medullary, forming nodose tumors from the size of a hen's egg to that of a child's head, and seated in one of the lobes of the gland. It is usually surrounded by normal gland-tissue or adenomatous tissue. Rarely is the whole gland transformed to cancer-tissue. Secondary growths, and irruptions into the trachea or larynx, are common; but both are often absent for a long space of time, the tough cortical substance of the gland offering considerable resistance to the advancing growth.

WÖLFLER distinguishes three forms of carcinoma—alveolar, columnar-celled, and squamous-celled. **Alveolar** carcinoma is the commonest, and occurs as grayish nodes surrounded by fibrous tissue and seated in the parenchyma of the gland, or as a uniform medullary infiltration of the goitrous tissue. The proliferous epithelial cells are usually rounded or oval, or sometimes polymorphous; they form globular or elongated masses or nests separated by fibrous bands of varying thickness. Between the nests we frequently find persistent remnants of normal follicles. The development of the growth begins in the epithelial cells which lie 'unutilized' or form compact masses between the gland-follicles. The lining epithelium of the follicles takes no part in the development of the cancer, which thus in its mode of growth recalls the gelatinous adenoma in which it often originates: it is indeed distinguishable from the latter only by the fact that no trace of reversion to any glandular type appears in it. The old gland-follicles often persist for a long time amid the advancing growth, but are ultimately encroached on or filled up by the new-formed cancer-cells. **Columnar-celled** carcinoma corresponds in structure to the columnar-celled parts of the normal gland and to columnar-celled adenoma. It takes the form of nodes whose cut surface is white or grayish-red. The neoplastic tissue is characterized by the presence in it of solid cords of cells, and of tubules and follicles clothed with cylindrical epithelium and containing papillary ingrowths exactly resembling those of papillary cyst-adenoma. WÖLFLER regards this form also as originating in the interacinous epithelial cells. **Squamous-celled** carcinoma is a rare form (FÖRSTER, EPPINGER, LÜCKE, KAUFMANN, BRAUN). As there is normally no squamous epithelium in the thyroid it is not improbable that, in cases where the growth does not start from the œsophagus, it is due to the morbid development of embryonic epithelial cells accidentally enclosed in the gland on the closure of the branchial clefts.

Of the **connective-tissue tumors** of the thyroid **sarcoma** is the commonest, and usually originates in an already-existing goitre. Both

round-celled and spindle-celled sarcoma are described, and Wölfler adds to the list of forms—giant-celled sarcoma, angiosarcoma, and alveolar sarcoma. They form irregular nodulated tumors extending over a part or the whole of a single lobe, seldom over the entire gland. The cut surface is generally smooth, though the tumor is usually more or less lobulated by the bands of firm fibrous tissue which traverse it. The tint is white or grayish, pink, reddish-brown, or dark-brown, according to the amount of blood present. The latter tint prevails where there are cavernous blood-vessels with hæmorrhagic infiltrations. The tumor is more or less firm according as it is fibrous or cellular: the round-celled form is the softest. The acini surrounded by neoplastic tissue often survive a long time. Tumors are described in which muscle-fibres appeared to be included. Secondary growths are set up in consequence of invasion of the lymphatics or blood-vessels. Sarcoma occurs in patients of all ages.

Wölfler describes a case of **fibroma** in a man of 56; it took the form of multiple hard nodes of about the size of a walnut.

Carcinoma and sarcoma of the thyroid are often included under the term malignant goitre (*struma maligna*).

References:—Virchow, *op. cit.*; Eberth, *Virch. Arch.* vol. 55; Eppinger, *Prager Viertelj.* 1875; Kocher, *D. Zeitschr. f. Chir.* IV.; Kaufmann, *ibid.* XI., XIV.; Lücke, *Arch. f. klin. Chir.* VIII.; Rose, *ibid.* XXIII., W. Müller, *Jena Zeitschr. f. Med.* VI. 1871; von Winiwarter, *Beitr. z. Statistik d. Carcinoma* Stuttgart 1878; Cornil, *Arch. de physiol.* 1875; Payne, *Trans. Path. Soc.* XXII. 1871; Demme, *Jahresber. d. Berner Kinderspitals* 1879 and *Gerhardt's, Handb. d. Kinderkr.* III.; Griffini, *Arch. per le scienze med.* IV. 1880; Pinner, *D. Zeitschr. f. Chir.* XVII. 1882; Braun, *Langenbeck's Arch.* XXVIII.; E. Neumann, *ibid.* XXIII.; Bircher, *Sammlung klin. Vorträge* 222; Heath, *Med. Times* 1879; Huguenin, *Arch. d. Heilk.* XV. 1874; Wölfler, *loc. cit.*; Haward, *Trans. Path. Soc.* XXXIII. 1882.

623. In all forms of goitre certain retrogressive changes are apt to take place, and these to a greater or less extent alter the appearance of the growth.

Hæmorrhages are common, either in the form of small ecchymoses or of large extravasations extending over the greater part of the tumor and giving it a dark-brown tint. They sometimes constitute a large portion of its bulk, and when they occur within thin-walled cysts may lead to their rupture. These extravasations also lead to wide-spread disintegration and necrosis of the tissue of the tumor, forming foci of brown or yellow softening which ultimately take the form of cysts. As we mentioned in Art. 621 small extravasations may be followed by proliferation of the glandular parenchyma and formations of hyaline or fibrous tissue. If the fibrous overgrowth be marked indurations and cicatrices result, and these sometimes become in course of time calcified.

When the goitrous tissue disintegrates in consequence of hæmor-

rhagic infiltration **fatty change** often sets in round about the affected area, and oil-globules mingle with the necrotic detritus and disintegrated blood-cells; when the fatty change is marked this may give the pulpy contents of the softened patch a creamy or yellowish-white color. The tissue enclosing the patch is usually more or less inflamed, and as the detritus is gradually absorbed a cyst-wall of indurated fibrous tissue is developed.

Hæmorrhage, necrosis, and fatty degeneration of this kind, together with the inflammatory changes that accompany these, are the commonest causes of the **fibroid degeneration** and induration so frequently met with in goitres. When these changes affect the central parts they give rise to large white radiating cicatrices. Where hæmorrhages have been frequent a more diffuse induration is set up, which is then apt to spread over the whole tumor and cause the degeneration and atrophy of the glandular elements. The new-formed fibrous tissue is usually white and lustrous, often resembling hyaline cartilage.

Calcareous deposits occur in the gland-tissue as well as in the new-formed fibrous tissue, and are first seen in the colloid masses contained in the acini and in the interacinous tissue. In advanced cases the entire contents of the acini are transformed into shining stratified calcareous grains. In the interacinous tissue the deposit is most marked where fibrous hyperplasia has occurred, and it is consequently by no means uncommon to find the indurated parts transformed into gritty masses and the cysts of disintegration enclosed by capsules that are completely calcified. FÖRSTER and LÜCKE describe cases in which the fibrous tissue has become ossified.

A very common occurrence in goitrous tumors is the excessive development of **colloid substance,** especially when the interacinous vessels are few and narrow. The colloid substance is secreted by the epithelium in the form of clear colorless droplets, and the detached epithelial cells are themselves transformed into similar hyaline masses. When the secretion is exceptionally abundant the tumor consists almost entirely of a translucent honey-like substance lying in masses separated only by thin fibrous septa. This form is described as **gelatinous goitre** (*struma gelatinosa*). WÖLFLER describes it as a parenchymatous atrophy of the gland, and regards it as an advanced stage of gelatinous adenoma: he supposes that the intra-acinous elements are transformed into colloid substance, while the interacinous tissue becomes atrophied.

So-called **multilocular cystoma** probably arises in the same way: the atrophy of the interacinous tissue and its vessels goes on almost to complete disappearance, and the follicles thus come together and coalesce.

When the secretion of colloid substance is very rapid some of the acini may burst, and their contents pass into the surrounding tissue. This tissue is thus disintegrated and destroyed, and a cyst is formed contain-

ing colloid material and frequently extravasated blood. In other cases cicatricial tissue is developed. Sometimes an over-distended acinus ruptures through the skin or into the larynx or trachea.

Amyloid degeneration takes place in thyroid glands otherwise normal, and also in goitres: it chiefly affects the blood-vessels. Local amyloid deposits are also met with in the form of lardaceous or waxy nodes (BECKMANN).

Acute **inflammation** of the normal or goitrous gland (thyroiditis, and acute strumitis) occurs as a result of traumatic injury, of septic or pyæmic infection, after typhoid, diphtheria (BRIEGER), and rheumatism; it may also arise idiopathically, and causes more or less painful swelling of the part. If suppuration takes place one or more pus-cavities or abscesses or even patches of gangrene result, and these may rupture into surrounding parts. Chronic inflammation and induration are usually due to internal necroses: other forms are very rare.

Tuberculosis of the thyroid gland is not very common, though in hæmatogenous miliary tuberculosis eruptions of tubercle are met with in it; larger tuberculous foci have also been described.

Gummata of the thyroid are very rarely met with.

References on **thyroiditis** and strumitis:—BECK, *Arch. f. physiol. Heilk.* 1851; BAUCHET, *Gaz. hebd.* 1857; MARTINACHE, *De l'inflam. aiguë du corps thyr.* Paris 1861; CHANTREUIL, *Gaz. des. hôpitaux* 1866; STAUDENMEYER, *Zeitschr. f. chir. Med. u. Geburtsh.* 1870; KOCHER, *D. Zeitschr. f. Chir.* X.; ROELLINGER, *De la thyr. aiguë* Paris 1877; BÖGEHOLD, *Deut. med. Woch.* 1880; PUICHAUD, *Paris médical* 1881; WEIGERT, *Virch. Arch.* vol. 83 (tuberculosis); CHIARI, *Stricker's med. Jahrb.* 1878 (tuberculosis); VIRCHOW, *op. cit.*; DEMME, *loc. cit.*; WÖLFLER *op. cit.*; DUMOLARD, *Lyon médical* 44. 1878; BRIEGER, *Charité-Annalen* VIII. 1883 (diphtheria); CORNIL and RANVIER, *Man. Path. Hist.* I. London 1882 (tuberculosis); BARTH and GOMBAULT, *Progrès médical* 1884 (syphiloma).

623 *a*. The **ætiology of goitre** is at present imperfectly understood, but we know something at least of the conditions under which it usually appears. We have already seen (Art. 621) that increased flow of blood to the thyroid body, or obstruction of the flow from it, may occasion a very marked swelling of the gland. Such a swelling is not always transient, but sometimes leads to permanent enlargement from dilatation of the vessels and hyperplasia of the gland-tissue. Excessive use of the voice, blowing of wind-instruments, carrying heavy loads, frequent ascending of steep hills, frequent sexual excitement, menstruation, pregnancy, infective diseases, heart-disease, etc. may all act in this direction. A striking instance is the chronic enlargement of the gland from persistent congestion in the peculiar vaso-motor disorder known as Graves' or Basedow's disease (**exophthalmic goitre**); a disease characterized by increased rapidity of the heart's action, increased pulsation in the arteries of the neck and head, and protrusion of the eyeballs from the orbits. If a goitrous tumor can be thus produced it is natural to regard it as due to

the increased blood-supply of the organ, which leads to increased nutrition and therefore hypertrophy of the gland-tissue. Such goitres are always found to be highly vascular.

But hyperæmia alone is not enough to account for all goitres, and it fails entirely to explain the fact that goitre prevails much more in some regions than in others. In certain regions indeed a large proportion of the inhabitants are goitrous. Moreover it is observed that families hitherto free from goitre acquire the disease when they move into regions where it is common, and that goitrous patients lose the disease when they are removed to regions where it is unknown. These facts require us to assume that the conditions which favor goitre are to some extent local. This view is corroborated by the fact that even in regions where goitre is endemic there are occasionally regular epidemics of the disease, in which *e. g.* the inmates of garrisons or of institutions simultaneously suffer from rapidly growing thyroid tumors.

This endemic and epidemic mode of occurrence has been accounted for in the most various ways: the air, the soil, the water, the social conditions, all have at one time or another been accused. None of these theories however have met with general acceptance. The most probable explanation seems to be that the local exciting cause of goitre is of a miasmatic nature, independent of the altitude and of the temperature of the region, but developing only over certain kinds of rock or soil. Bircher, one of the latest writers on the subject, concludes from his minute researches on the distribution of goitre in Switzerland, where the disease is in many parts endemic, that it occurs only on marine deposits of palaeozoïc, triassic, or tertiary age; while eruptive volcanic rocks, the older crystalline formations, jurassic and calcareous deposits, and fresh-water deposits generally, are exempt.

The exact nature of the miasma, and its mode of entrance into the body, are as yet unknown. Klebs and Bircher suspect the existence of some specific micro-organism, though they have not succeeded in obtaining any experimental basis for the supposition. It will very probably be found that the exciting agent enters the body in drinking water. We are also unaware of the manner in which the exciting agent works, but it is not unlikely that it sets up hyperæmic conditions in the thyroid. As infants are sometimes born goitrous, we must assume that it may pass from mother to fœtus and influence the latter within the womb. Epidemics of goitre in goitrous regions indicate that at certain times the conditions favoring infection are exceptionally intense, and cause either an unusual development of the miasma or a temporarily increased predisposition on the part of the persons affected.

In places where goitre is endemic, deaf-mutes, idiots, and so-called cretins are exceptionally numerous. **Cretinism** is a disorder of development essentially affecting the growth of the bones, but accompanied also by morbid changes in the soft parts. These forms of imperfect

development have often been correlated with the occurrence of goitre; and it has been suggested that cretinism may be due to the miasma which induces goitre, the latter being as it were a milder form of the same disorder.

BIRCHER formally states his belief that endemic goitre, endemic deaf-mutism, cretinism, and cretinoid idiocy are all due to one and the same miasma. Further research is required before this view can be either accepted or rejected. It has in its favor the fact that cretins and cretinoid idiots are usually also goitrous, and that they are more numerous in regions where goitre is endemic.

HORSLEY (*Brown Lectures, Brit. Med. Journ.* 1, 1885) has shown experimental evidence for the view that cretinism, as also the peculiar cachexia which occasionally follows the extirpation of a goitre (*cachexia strumipriva*), and **myxœdema** are consequences of arrest of the function of the thyroid gland. By removing the gland he succeeded in producing in monkeys a cretinoid state, characterized by hebetude, malnutrition, muscular tremor, puffy œdema, leucocytosis, and the presence of mucin in the blood and connective tissues. Myxœdema in the human subject is a state having the same general characters, and it is associated with wasting of the thyroid gland or its destruction by a new growth.

References :—VIRCHOW, *Gesammelte Abhandl.* 1856; ST. LAGER, *Étude sur les causes du crétinisme et du goître endémique* Paris 1867; LÜCKE, *Pitha u. Billroth's Chirurgie* III.; BAILLARGER, *Enquête sur le goître et le crétinisme* Paris 1873; DEMME, *loc. cit.*; FREUND, *Die Bezieh. d. Schilddrüse zu d. weibl. Geschlechtsorganen* In. Diss. Strasburg 1882; KLEBS, *Stud. üb. d. Verbreitung d. Kropfes in Oesterreich* Prague 1878; RÖLL, *Spec. Path. und Therap. d. Hausthiere* 1876; HIRSCH, *Handb. d. histor. geograph. Path.* II. 1883, trans. by CREIGHTON (New Syd. Soc.) II. London 1885 (with ample references to the literature of the subject); BIRCHER, *Der endemische Kropf* Basle 1883; KRATTER, *Der alpine Cretinismus* Graz 1884; HILTON FAGGE *Prin. and pract. of med.* I. London 1886.

On the *cachexia strumipriva*, surgical and experimental, see KOCHER, *Arch. f. klin. Chir.* XXIX. 1883; REVERDIN and SCHIFF, *Rev. méd. de la Suisse romande* 1883-84; WAGNER, *Wiener med. Blätter* 1884; SANQUIRICO and CANALIS, *Arch. p. l. sci. med.* VIII. 1884; BRUNS, *Sammlung klin. Vorträge* 244; JULLIARD, *Revue de chirurgie* 1883; BAUMGÄRTNER, *Arch. f. klin. Chir.* XXXI. 1884; GRUNDLER, *Zur Cachexia strumipriva* Tübingen 1884; ZESAS, *Deut. Medicinalzeitung* 1885; ALBERTONI and TIZZONI, *Cent. f. med. Wiss.* 24, 1885; FUHR, *Arch. f. exp. Path.* XXI. 1886 (with a discussion of the literature).

For cases of myxœdema see GULL, *Trans. Clin. Soc.* VII. 1879; ORD, *Med. chir. Trans.* XLIII. 1878, *Trans. Clin. Soc.* VIII. 1880; DYCE DUCKWORTH, *ibid.*; CAVAFY, *ibid.* XV. 1882; HARLEY, *Med. chir. Trans.* LXVII. 1884; Discussion, *Brit. Med. Journ.* 2, 1883; WHITE, *Lancet* 1, 1885.

CHAPTER XC.

THE THYMUS GLAND.

623 *b*. The **thymus** is a gland-like body, which grows to a considerable size in the fœtus and during the first two years of infancy: after that however it ceases to grow, and about the tenth year undergoes retrograde change into fibrous and adipose tissue.

It lies in the superior mediastinum behind the first piece of the sternum, extends upwards nearly to the thyroid, and is made up chiefly of two flat elongated lobes which are in contact or coherent along their medial borders and are enclosed in a thin connective tissue. The lobes are subdivided into lobules by fibrous septa. The structural units or acini closely resemble lymphatic glands, and are composed of a loose reticular or adenoid stroma, filled with indifferent or lymphoid elements and larger multinuclear cells. In the peripheral parts of the acinus the stroma is somewhat closer and more densely filled with cells than in the centre, and thus a cortical and a medullary layer are distinguished. The thymus possesses no duct, but it has numerous lymphatics whose exact course is however only imperfectly understood.

Small **accessory glands** are not uncommon; they usually lie above the gland and near the thyroid. Congenital absence of the gland occurs only in highly malformed fœtuses.

The weight of the thymus in a new-born infant is about 14 grammes; in a child of two it is about 26 grammes: this is subject however to considerable variation.

According to STIEDA, KÖLLIKER, HIS, and WATNEY, the thymus develops from the epithelium of a branchial cleft, and is thus originally an epiblastic or epithelial structure. The epithelial cells however disappear after a time, and the development of the characteristic lymphadenoid tissue starts from mesoblastic (connective-tissue) elements.

The **function** and exact significance of the thymus is not certainly known. WATNEY, who has made it the subject of extensive investigation, thinks that it takes part in the formation of red and white blood-cells. The former are supposed to be developed in certain nucleated cells containing hæmoglobin.

Before birth, and in larger numbers during infancy, the thymus contains homogeneous or indistinctly-laminated partially-calcified bodies known as Hassall's concentric corpuscles. They lie chiefly in the centre

of the acini, and are composed of cells closely applied to each other like the coats of an onion. STIEDA regards these as the remains of the rudimental epithelial structures; AMMANN thinks they develop from the stroma-cells or the perithelium of the blood-vessels, or from lymphoid elements whose nucleus and protoplasm have undergone colloid degeneration. The laminated bodies, calcified and uncalcified, break down and disappear during the retrogression of the gland, which is manifested chiefly by the dwindling and disappearance of its cells.

Of **morbid changes** in the thymus the commonest is imperfect retrogression, by which it sometimes persists till the thirtieth or fortieth year.

Hæmorrhage into the gland is met with chiefly in asphyxia, or in connection with the hæmorrhagic diathesis (BOUCHER *Bull. de la soc. anat.* II. 1857; ACLAND, *Lancet* 2, 1884 and *Trans. Path. Soc.* XXXVI. 1885).

Hæmatogenous purulent inflammation is usually due to pyæmia and may lead to multiple abscesses or to general suppuration. Suppuration affecting the structures of the neck is apt to extend to the thymus. Nothing is known of chronic indurative change in the gland.

Tuberculosis appears in the form of disseminated nodules, and of large caseous foci.

Gummatous inflammatory change due to syphilis has been several times described.

Primary tumors having the structure of soft or hard lymphosarcoma or of simple sarcoma occur in connection with general leukæmia and also independently. They appear as soft and marrowy or sometimes moderately firm growths, and at times reach a considerable size. They may compress the air-passages or blood-vessels, or displace the heart or lungs.

References:—KÖLLIKER, *Gewebelehre* Leipzig 1867, and *Entwickelungsgeschichte* Leipzig 1879; AFFANASIEW, *Arch. f. mikrosk. Anat.* XIV. (1877); FRIEDLEBEN, *Die Physiol. d. Thymusdrüse* Frankfort 1858; HIS, *Zeitsch. f. wiss. Zoologie* X., XI., and *Menschliche Embryonen* I. Leipzig 1880; STIEDA, *Unters. üb. d. gland. thymus, gland thyr. und gland. carotica* Leipzig 1881; VIRCHOW, *Virch. Arch.* vol. 3; GEGENBAUR, *Anatomie* Leipzig 1883; WATNEY, *Phil. Trans.* III. 1882; AMMANN, *Beitr. z. Anat. d. Thymus* In. Diss. Basle 1882; DUBOIS, *Gaz. méd. de Paris* 1850 (inflammations); DEPAUL, *Mém. d. l'acad. de. méd.* XVII. (inflammations); EBERTH, *Virch. Arch.* vol. 40 (gumma); LANCEREAUX, *Traité d'anat. path.* II. Paris 1881; VIRCHOW, *Krankhafte Geschwülste* II.; WITTICH, *Virch. Arch.* vol. 8 (lymphoma); STEUDENER, *ibid.* vol 59 (sarcoma); HAHN and THOMAS, *Arch. générales* 1879; HEDENIUS, *Nord. med. Arkiv* 24, 1878.

SECTION XI.

THE CENTRAL NERVOUS SYSTEM.

CHAPTER XCI.

STRUCTURE AND FUNCTIONS.

624. The **central nervous system** consists of the spinal cord, the cerebral axis, and the cerebrum. These parts are made up of nerve-cells and nerve-fibres, together with a framework of connective tissue which carries the nutrient vessels. The nerve-cells or ganglion-cells are for the most part aggregated in masses which are known as nerve-centres or gray nuclei. The nerve-fibres form either plexuses or tracts, and serve to connect the ganglion-cells of one group with those of another or with the peripheral terminations (end-organs) of certain nerves.

The cord and the cerebral axis contain centres of subordinate importance, forming as it were intermediate stations between the central and peripheral extremities of the nerve-tracts. The cerebrum is the central terminus with which the peripheral sensory and motor end-organs are connected either directly or through the intermediate stations.

The **cerebrum** consists of two hemispheres connected by a commissure, the *corpus callosum*. The outer surface of the hemispheres is thrown into a series of complicated convolutions consisting of ridges and furrows (*gyri* and *sulci*), the latter ramifying and intercommunicating in a remarkable way.

Some of the sulci are characteristic of the human brain, and are always present; others vary in different brains, and thus the configuration of the convolutions is by no means absolutely constant. The most important sulci are—the **sylvian** fissure (Fig. 243 *e*), the **central** or rolandian fissure (*a*), the **præcentral** or transverse-frontal furrow (*b*), the **intraparietal** furrow (*d*), the **first-temporal** or parallel furrow (*f*), the **parieto-occipital** furrow (*c*), the **anterior-occipital** furrow (*i*), and the **inferior-occipital** furrow (*h*).

The central fissure divides the cerebral hemisphere into an anterior and a posterior portion; the (central) convolutions which form its anterior and posterior borders are known as the anterior-central or **ascending-frontal** (*A*), and the posterior-central or **ascending-parietal** (*B*). The portion of the hemisphere in front of the central fissure is the **frontal lobe,** and includes the ascending-frontal (*A*), the superior frontal (C_1), middle-frontal (C_2), and inferior-frontal (C_3) convolutions. The last three convolutions all pass round to the orbital surface of the hemisphere.

Immediately behind the ascending-parietal convolution (B), and divided from it by the intraparietal furrow (d), lies the superior-parietal lobule (D); the inferior-parietal lobule being made up of the marginal (or supramarginal) convolution (E) and the angular convolution (F). These ($BDEF$) constitute the **parietal lobe.**

The parieto-occipital furrow (c) and the anterior-occipital furrow (i) separate the parietal from the **occipital lobe** (G), and in the space between the two furrows the so-called annectant (or connecting) convolutions pass over from the parietal lobe to the occipital lobe.

The sylvian fissure (e) forms the boundary between the outer and lower portions of the frontal and parietal regions and the **temporal lobe.** The convolution bordering the lower side of the fissure is the first-temporal or superior temporo-sphenoidal (H_1). The convolution

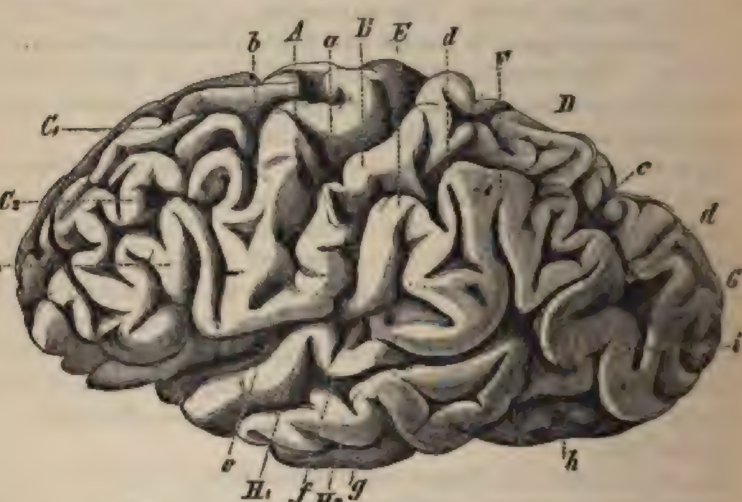

FIG. 243. OUTER SURFACE OF THE LEFT CEREBRAL HEMISPHERE.

(*From a brain hardened in nitric acid and dried.*)

a, central or rolandian fissure
b, præcentral furrow
c, parieto-occipital furrow
d, intraparietal furrow
e, sylvian fissure
f, first-temporal or parallel furrow
g, second-temporal furrow
h, inferior-occipital furrow
i, anterior-occipital furrow

A, ascending-frontal convolution
B, ascending-parietal convolution
C_1, superior-, C_2 middle-, C_3 inferior-frontal convolution
D, superior-parietal lobule
E, marginal convolution, F, angular convolution } inferior-parietal lobule
G, occipital lobe
H_1, first-temporal, H_2 second-temporal, convolution.

which curves round the upper end of the sylvian fissure is assigned to the parietal lobe and is called the marginal convolution (E). Beneath the first-temporal convolution lies the first-temporal or parallel furrow (f), and beneath that the second-temporal convolution (H_2). Springing from the upper part of the latter convolution the angular gyrus or

convolution (F) curves round the end of the first-temporal furrow (f): it also is assigned to the parietal lobe. Beneath the second-temporal furrow (g) lies the third-temporal convolution (Fig. 244 t^3).

If next the lips of the sylvian fissure be separated the **central lobe** or island of Reil becomes visible.

The **median surface** of the superior-frontal convolution (mF^1) has no special name: the median surface of the ascending (frontal and parietal) convolutions that border the central fissure is called the paracentral lobule (*Parc*). Both are bounded inferiorly by the calloso-marginal fissure (*cm*), which anteriorly separates the superior-frontal convolution from the convolution of the corpus callosum (*gyrus fornicatus*

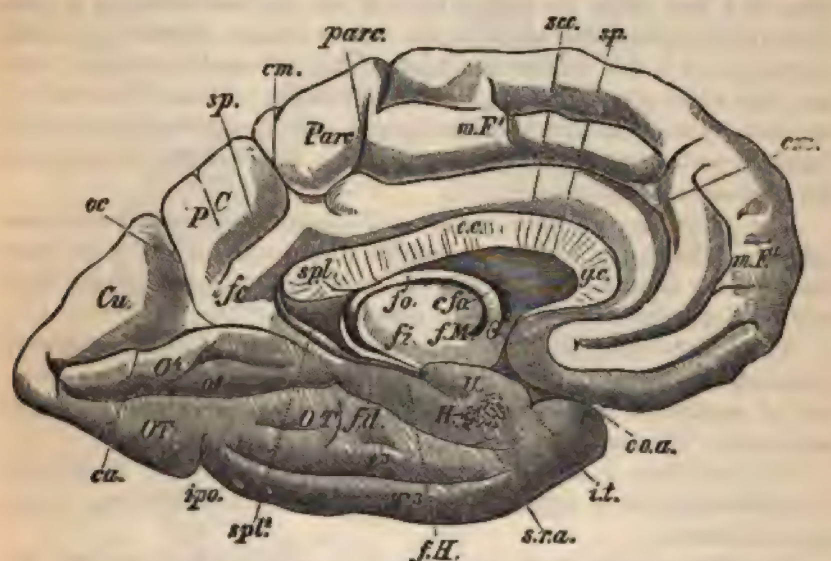

FIG. 244. MEDIAN SURFACE OF THE LEFT CEREBRAL HEMISPHERE (*after* SCHWALBE).

cm, calloso-marginal fissure
scc, sulcus of the corpus callosum
oc, parieto-occipital furrow
sp, subparietal furrow
s.p., septum lucidum
ca, calcarine fissure
ipo, *incisura præoccipitalis*
ot, occipito-temporal (or collateral) furrow
t, third-temporal furrow
fH, hippocampal (or dentate) fissure
it, *incisura temporalis*
cc, corpus callosum
gc, genu
spl, splenium
fo, fornix
cfo, anterior pillar (columna) of the fornix
coa, corpus albicans
mF^1, superior-frontal convolution
H, hippocampal gyrus
Parc, paracentral lobule
PC, quadrate lobule (præcuneus)
Cu, cuneus
O^1, uncinate gyrus (lingualis)
OT, occipito-temporal convolution
T^3, third-temporal convolution
U, uncus of uncinate gyrus
fd, fascia dentata
fi, fimbria
fM, foramen of Monro
sra, substantia reticularis alba
fc, gyrus fornicatus or convolution of the corpus callosum

or *cinguli fc*), and posteriorly separates the paracentral lobule from the quadrate lobule (or *præcuneus PC*), the median portion of the superior-

parietal lobule. The median portion of the occipital lobe is called the *cuneus* or cuneate lobule (*Cu*), and is parted from the quadrate lobule by the parieto-occipital furrow (*oc*).

The calcarine fissure (*ca*) separates the cuneus from the uncinate gyrus (*gyrus lingualis O'*); the latter passes forward and becomes the hippocampal gyrus (*H*).

Beneath the uncinate gyrus lies the occipito-temporal or collateral furrow (*ot*), and beneath this the occipito-temporal convolution (*gyrus fusiformis OT*).

625. The mass of the cerebrum consists of cortical or gray matter (Fig. 245 *co*) and medullary or white matter. The former is of a soft-gray tint and forms the surface layer of all the convolutions; it also occurs at the base of the brain in the masses known respectively as the claustrum (*cl*), the nucleus amygdalæ (*na*), the caudate nucleus (*nc*), and the outer portion of the lenticular nucleus. These latter are all connected anteriorly with one another and with the cortical gray matter (anterior perforated space). Posteriorly they are separated by intervening portions of white matter.

The gray masses known as the optic thalamus or simply thalamus (*th*), the subthalamic body or nucleus of Luys (*cs*), and the inner two-thirds of the lenticular nucleus (*nl*) do not strictly lie within the cerebral hemispheres but belong to the cerebral axis.

The cortical **gray matter** consists of a delicate fibrous meshwork (neuroglia) which in the dead brain is finely granular, enclosing a number of multipolar ganglion-cells, and nerve-fibres of various thickness arranged in plexuses and tracts.

The medullary or **white matter** is composed chiefly of medullated nerve-fibres devoid of primitive sheaths, all of them originating in the gray substance.

The fibres starting from the cortex form bundles which pass into the white *centrum ovale* of the hemisphere. Those from the central region form the *corona radiata*, and for the most part pass down to the base of the brain; the others connect the various convolutions with one another and are spoken of as associating or interconnecting fibres.

Some of these bundles or tracts have received special names: adjacent convolutions are connected by the *fibræ propriæ* (GRATIOLET); the orbital convolutions of the frontal lobe are connected with the anterior parts of the temporal lobe by the fibres of the uncinate fasciculus, which passes across the bottom of the sylvian fissure; the corpus callosum connects corresponding cortical regions in the two hemispheres; the anterior (or white) commissure connects the two olfactory lobes and the two temporal lobes; the arcuate fasciculus consists of fibres passing over the corpus callosum from the frontal lobe to the occipital lobe; and so on.

The **cortex** is the terminal station for all nerves. Every part of the sensorial surface of the body and the whole muscular system are con-

nected by nerve-tracts (the 'projective system') with the cortex. By means of these tracts impressions corresponding to every sensory stimulus and to every muscular movement are conveyed to the cortex; and these impressions probably leave traces of 'memories' in the ultimate structure of the gray matter (MEYNERT). These traces or memories form the physical substratum of our psychical existence, of our consciousness. The traces are not diffused indiscriminately over the surface of the brain, but tend to become associated with certain parts; and thus the various sensory surfaces and the various groups of muscles come into definite relation with certain definite regions of the cortex. These

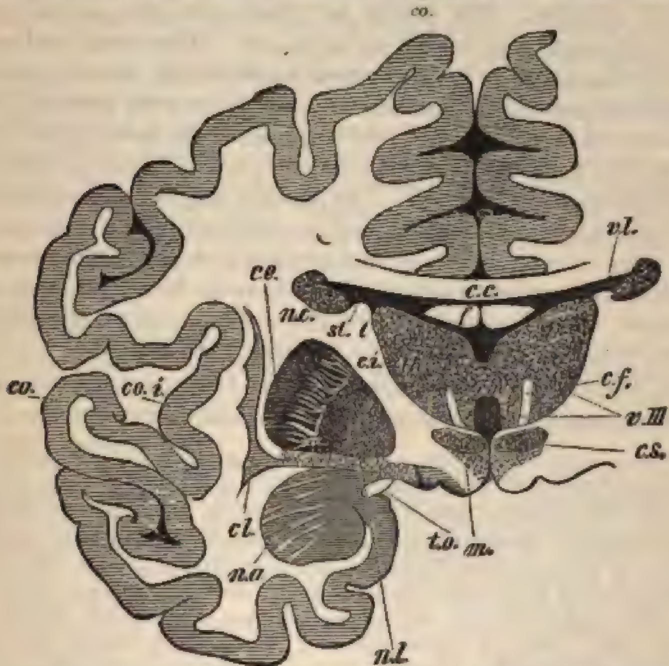

FIG. 245. DIAGRAMMATIC TRANSVERSE VERTICAL SECTION OF THE CEREBRUM (*after SCHWALBE*).

co, cortex	*ci*, internal capsule
coi, island of Reil	*ce*, external capsule
cl, claustrum	*stt*, stria terminalis (tænia semicircularis)
na, nucleus amygdalæ	*cf*, anterior pillar of the fornix
nc, caudate nucleus	*f*, fornix
th, optic thalamus	*cc*, corpus callosum
cm, middle commissure	*vIII*, third ventricle
cs, subthalamic body	*vl*, lateral ventricle
m, substantia nigra	*to*, optic tract
nl, lenticular nucleus	

cortical centres or areas are however not sharply circumscribed, but encroach upon one another at many points.

The researches of BOUILLAUD, BROCA, MEYNERT, KUSSMAUL, HUGHLINGS-JACKSON, HITZIG, FRITSCH, FLECHSIG, WERNICKE, MUNK, FERRIER, CHARCOT, HUGUENIN, PITRES, LÉPINE, MARCACCI, BAUM-

LER, EXNER, TRIPIER, PETRINA, KAHLER, PICK, and others have determined the position of these areas or centres for various functions and movements, and this not only in man but in a number of other animals. Thus it is almost certain that the centre for the co-ordination of the movements of speech is placed chiefly in the inferior-frontal convolution on the left side, and the centre for auditory perception in the first-temporal convolution. Destruction of the former centre involves the loss of power to perform the movements necessary for articulate speech (aphemia or motor aphasia); and on destruction of the latter centre the patient is unable to understand spoken words (word-deafness or sensory aphasia). The centre for visual perception appears to lie chiefly in the angular gyrus and occipital lobe. The motor and sensory centres for the limbs lie in the central convolutions (ascending-frontal and ascending-parietal), the paracentral lobule, and the parts adjoining.

FLECHSIG divides the surface of the brain into three great regions having distinct functions—they are the frontal zone, the parietal zone, and the temporo-occipital zone. The parietal zone contains the starting-points of the direct motor tracts and the terminal-points of most of the sensory tracts: it may therefore be described as the sensory-motor zone. The frontal and temporo-occipital zones have no direct relations to the motor tracts, but are connected with the optic thalamus, the pons, and the cerebellum. Both zones are, he considers, in close relation with the psychical processes, and the parts of them bordering on the parietal zone have an important connection with the function of speech.

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626. The **spinal cord** is an elongated cylindrical body, somewhat flattened antero-posteriorly, and composed of gray matter and white matter. The **gray matter** is in the interior, extending throughout the length of the cord, the cross-section being roughly H-shaped (Fig. 246) and forming two **anterior horns** (*or cornua, ca*) and two **posterior horns** (*c p*), united by a gray commissure. The commissure contains the **central canal** (*cc*), a slender tube lined with epithelium. The

anterior horns are of larger sectional area than the posterior, but their size and configuration vary remarkably in different parts of the cord: they are smallest in the dorsal region.

In numerous places, especially about the region midway between the anterior and posterior horns, radiating processes of gray matter pass into the white (near *c l*), and are known as *processus reticulares*. They interlace and form a network enclosing portions of white substance in its meshes. In the cervical and upper dorsal regions a lateral projection of the anterior horn appears, and is called the **intermedio-lateral tract** or lateral horn (*c l*).

The gray substance contains a multitude of ganglion-cells and nerve-fibres of various thicknesses, enclosed in a delicate neuroglia. Round the central canal and at the extremity of the posterior horn the neuroglia

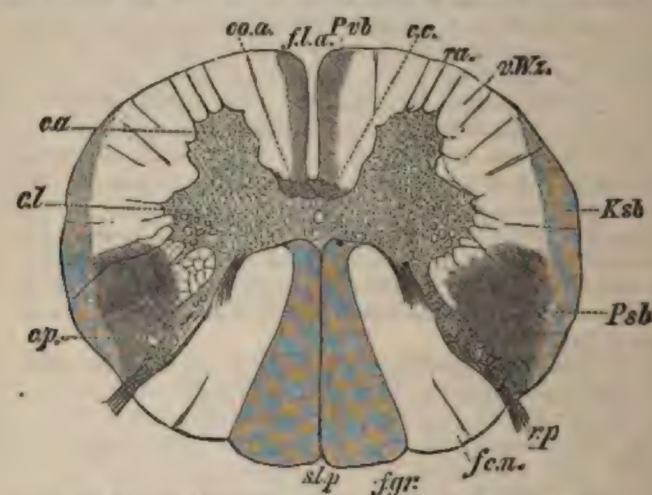

FIG. 246. DIAGRAMMATIC SECTION OF THE SPINAL CORD (× 6).

ca, anterior horn
cl, lateral horn (so-called)
cp, posterior horn
cc, central canal
coa, anterior or white commissure
fcn, funiculus cuneatus (posterior root-zone or column of Burdach)
Ksb, direct cerebellar tract
ra, anterior root
rp, posterior root
fla, anterior longitudinal fissure
slp, posterior longitudinal fissure
fgr, funiculus gracilis (column of Goll)
Psb, lateral (or crossed) pyramidal tract
Pvb, anterior (or direct) pyramidal tract (column of Türck)
vWz, anterior root-zone

is rich in cells, and ganglion-cells are absent: these parts are spoken of as the *substantia gelatinosa*, the parts containing ganglion-cells as the *substantia spongiosa*.

In the anterior horn the ganglion-cells (motor cells) are large and multipolar; they possess numerous processes, one long and unbranched is the axis-cylinder process, the others subdividing and interlacing into a delicate network of fibrils. The anterior ganglion-cells are gathered into clusters, corresponding apparently to the territories of the blood-

vessels. In the posterior horns they are much smaller and more uniformly distributed. Two longitudinal columns of bipolar ganglion-cells exist in the dorsal region of the cord, lying to the median side of the inner portion of the posterior horns and known as Clarke's vesicular columns; these contain ganglion-cells intermediate in size between those of the anterior and those of the posterior horns.

The **white matter** of the cord forms a sheath surrounding the gray columns and filling up their irregularities. It is cleft behind by the slender posterior sulcus or fissure (*slp*) which extends to the gray matter, and anteriorly by the wider anterior fissure (*fla*) which does not quite reach the gray matter but leaves a narrow white or anterior commissure (*coa*) to unite the lateral halves of the cord. The white matter consists of large and small medullated nerve-fibres (without the primitive sheath of Schwann) running for the most part longitudinally; only a few run horizontally or obliquely. These fibres are divided into bundles by fibrous and neurogliar dissepiments extending inwards from the surface. Externally the cord is covered with a thin layer of grayish neuroglia. Very few ganglion-cells are met with in the white matter.

The **roots** of the spinal nerves are bundles of fibres leaving the cord anteriorly and posteriorly in more or less parallel directions. The anterior root (*ra*) contains motor fibres and starts proximately from the anterior horn: the posterior root (*rp*) conveys centripetal or sensory fibres to the posterior horn. A certain number of anterior-root fibres and posterior-root fibres unite into a nerve, and to each pair of nerves corresponds a more numerous aggregation of ganglion-cells; consequently the cord is subdivided into a number of natural segments whose number corresponds to that of the spinal nerves.

The portion of white matter between the anterior fissure and the anterior root is called the **anterior column**; that between the anterior and posterior root on the same side is the **lateral column**; that between the posterior root and the posterior fissure is the **posterior column.**

The fibres passing into the roots are connected with the ganglion-cells of the anterior horn by means of the axis-cylinder process, with those of the posterior horn by the network of fibrils; in the latter the ganglion-cell processes and the nerve-fibres interlace. From the gray matter other nerve-fibres pass into the neighboring white columns, which either serve to connect parts of the gray matter on different levels or pass directly upwards to the base of the brain or the cerebrum.

The longitudinal columns are subdivided into various tracts according to their physiological function. The best-known are the anterior (or direct) and lateral (or crossed) pyramidal tracts (*Pvb, Psb*), the lateral or direct cerebellar tract (*Ksb*), the column of Goll or *funiculus gracilis* (*fgr*), and the posterior root-zone or *funiculus cuneatus* (*fcn*).

The **anterior pyramidal tract** (column of Türck) and the **lateral pyramidal tract** contain centrifugal or efferent fibres, and form the

direct path of communication between the gray matter of the parietal zone of the cerebral cortex and that of the anterior horns. They traverse the internal capsule (Fig. 245 *ci*) and the peduncular tract, the lateral tract passing to the opposite side at the decussation of the pyramids, and the anterior tract passing directly down on the same side and crossing at some point in the cord by means of the anterior commissure to join the anterior horn of the opposite side.

The anterior tract (*Pvb*) lies medially in the anterior column, the

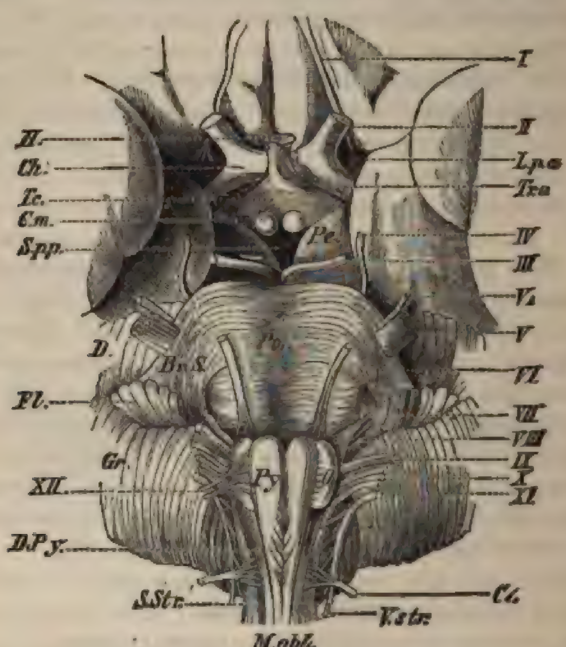

FIG. 247. BASAL ASPECT OF THE CEREBRAL AXIS

Mobl,	medulla oblongata	*H*,	stem of the hypophysis or pituitary body
Sstr,	lateral column	*TrO*,	optic tract
Vstr,	anterior column	*Ch*,	optic chiasma
Py,	pyramid	*I*,	olfactory nerve
DPy,	decussation of the pyramids	*II*,	optic nerve
O,	olivary body	*III*,	oculomotor nerve
Po,	pons	*IV*,	trochlear nerve
D,	anterior lobe of the cerebellum	VV_1,	trigeminus nerve
Gr,	digastric lobe of the cerebellum	*VI*,	abducens nerve
Fl,	flocculus of the cerebellum	*VII*,	facial nerve
BrS,	middle peduncle of the cerebellum	*VIII*,	auditory nerve
Pe,	crus cerebri (cerebral peduncle)	*IX*,	glossopharyngeal nerve
Spp,	posterior perforated space	*X*,	vagus nerve
Lpa,	anterior perforated space	*XI*,	spinal accessory nerve
Cm,	corpora albicantia (mammillaria)	*XII*,	hypoglossal nerve
Tc,	tuber cinereum with infundibulum	C_1,	anterior root of first cervical nerve

lateral tract (*Psb*) in the posterior part of the lateral column. The cross-section of each diminishes as we pass downwards from the medulla

The relative size of the crossed and uncrossed portions is very variable and in some cases unequal on the two sides, the section of the cord being then unsymmetrical. Usually the anterior tract disappears about the middle of the dorsal region. In some cases however it extends down to the lumbar region, and in others is entirely absent, that is to say the decussation at the pyramids is complete.

The **direct cerebellar tract** (*Ksb*) connects the gray matter of Clarke's column with the cerebellum. It runs along the outer margin of the posterior portion of the lateral column, and extends as far as the end of the dorsal region.

The remaining region of the anterior column is termed by FLECHSIG the **principal tract** of the anterior column, and that of the lateral column the **mixed lateral tract**. The fibres in these regions serve ap-

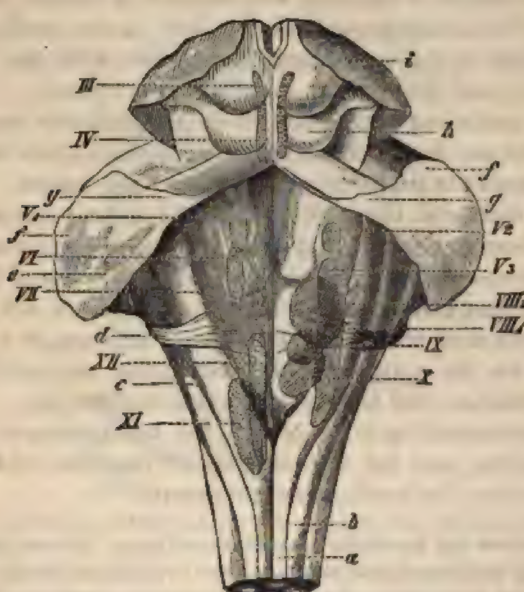

FIG. 248. DIAGRAM OF THE NUCLEI OF THE CRANIAL NERVES.

a, funiculus gracilis
b, funiculus cuneatus
c, restiform body
d, striæ acusticæ
e, posterior peduncle of the cerebellum
f, middle peduncle of the cerebellum
g, anterior peduncle of the cerebellum
h, corpora quadrigemina
i, crus cerebri

III, nucleus of the oculomotor
IV, nucleus of the trochlear
V_1, nucleus of the motor, V_2 V_3 nuclei of the sensory, root of the trigeminus
VI, nucleus of the abducens
VII, nucleus of the facial
$VIII_1$ $VIII_2$, nuclei of the auditory
IX, nucleus of the glossopharyngeal
X, nucleus of the vagus
XI, nucleus of the spinal accessory
XII, nucleus of the hypoglossal

parently to connect different portions of the gray matter of the cord with one another and with the brain, and include root-fibres which

The modifications which the cord undergoes in this region are chiefly these—the central canal becomes more and more posterior and is continued into the cerebral axis as the fourth ventricle, the aqueduct of Sylvius, and the third ventricle. At the same time the gray matter subdivides, and interpenetrating the white assumes a peculiar reticulated structure (Fig. 249 *Fr*) with numerous detached clusters of ganglion-cells from which the cranial nerves take their origin (Fig. 248).

This subdivision of the gray matter is accompanied by certain re-arrangements of the nerve-tracts. The pyramidal lateral columns cross each other at the decussation (Fig. 247 *DPy*), and pass to the ventral surface of the medulla (Fig. 248 *p*), while the shorter tracts connecting the several portions of the gray matter become less and less superficial. The column of Goll and the column of Burdach pass up (as the funiculus gracilis (Fig. 248 *a*) and funiculus cuneatus (*b*) respectively) to the lateral margin of the fourth ventricle, and together with lateral cerebellar tract and the arciform fibres of the restiform body (*c*) form the posterior peduncle of the cerebellum (*e*).

At this level fresh nuclei begin to appear, and form the substance of the olivary body (Figs. 247, 249 *o*), and the beginning of the gray matter of the cerebellum, corpora quadrigemina (Fig. 248 *h*), optic thalamus (Fig. 245 *th*), subthalamic body (*cs*), and numerous small masses (Fig. 249) embedded in the various columns and tracts. All these nuclei give rise in their turn to fresh bundles of fibres, some of which run in distinct tracts while others interlace with their neighbors.

Presently the longitudinal fibres are crossed by numerous arciform fibres (Fig. 249) some external (*fae*), others lying deeper (*Fr*, *b*) and forming a network (*formatio reticularis*) with the longitudinal fibres.

The cerebral axis may be considered as made up of three regions or strata (SCHWALBE)—the peduncular tract (MEYNERT, SCHWALBE), the tegmental region (FOREL), and the dorsal stratum.

The **peduncular tract** is in the **medulla** represented by the pyramidal columns (Fig. 249 *p*), which are surrounded and in part reinforced by the external arciform fibres (*fae*). The external arciform fibres enclose a nucleus known as the arciform nucleus (*nar*). In the **pons** the peduncular tract lies in the ventral stratum, being crossed and interlaced by the transverse arciform fibres derived from the middle peduncle of the cerebellum (Fig. 247 *BrS*). Some of these fibres are commissural and connect the two halves of the cerebellum; others penetrate the gray masses embedded among the arciform fibres and known as the nuclei of the pons. Certain of the nerve fibres which start from these nuclei join the bundles of pyramidal fibres and pass with them up to the cerebrum.

The bundles of pyramidal fibres, which in the pons are more or less subdivided and scattered, unite again into compact bundles on the anterior or cerebral side of the pons and, reinforced by the nuclear fibres

just referred to, form the pes or crusta of the **crura cerebri** (Fig. 247 *Pe*). The crusta is covered on the upper or dorsal surface by the substantia nigra, a layer of pigmented ganglion-cells, which in their turn give off fibres to join the crustal fibres. These latter then pass (mainly through the internal capsule) up to the cortex. The pyramidal fibres terminate in the ascending frontal and parietal convolutions and the parts adjoining, the other fibres pass to the frontal, temporal, and occipital lobes. A few enter the lenticular and caudate nuclei.

The **tegmental region** lies to the dorsal surface of the peduncular tract, and consists chiefly of the formatio reticularis (Fig. 249 *Fr*). The reticular structure is due to the subdivision into fibres of part of the gray matter of the anterior horn, with which are interlaced numerous arciform fibres. It includes in every part longitudinal fibres which are the continuation of the anterior and lateral columns of the cord, together with arciform fibres and scattered ganglion-cells. Posteriorly there is a so-called raphe (*r*), due to the decussation of some of the fibres in the middle line.

The tegmental portion of the **medulla** contains the nuclei of the twelfth, eleventh, tenth, ninth, and part of the eighth cranial nerves (Figs. 248, 249), the olivary nucleus (Fig. 249 *o*), the accessory olivary nuclei (*oam*, *oal*), the nucleus of the funiculus gracilis (*ng*), the nucleus of the funiculus cuneatus (*nc*), and other nuclei. The restiform body (Fig. 248 *c*) also belongs to this region, through which pass fibres from the lateral cerebellar tract of the cord, from the olivary body, and from the formatio reticularis, to the cerebellum.

The tegmental portion of the **pons** contains the nuclei of the fifth, sixth, seventh, and part of the eighth cranial nerves (Fig. 248). Fibres pass from the cerebellum into the formatio reticularis through the anterior peduncle of the cerebellum.

The tegmental portion of the **crura cerebri** lies beneath the aqueduct of Sylvius and is connected with the corpora quadrigemina and the anterior medullary velum. Beneath the aqueduct lies the nucleus of the third and fourth cranial nerves (Fig. 248). The formatio reticularis which lies to the ventral side of these nuclei contains (in addition to longitudinal bundles of fibres from the anterior and lateral columns of the cord) fibres from the corpora quadrigemina and anterior medullary velum, and from the cerebellum. The former proceed to the pons by way of the arcuate fibres, the latter by way of the anterior peduncles. The bundles from the cerebellum enclose in the part beneath the anterior corpora quadrigemina a reddish island of gray matter known as the red nucleus. Many of the fibres of these bundles terminate in this nucleus (GUDDEN), a few are seen to pass beyond it (FLECHSIG). These latter fibres pass to the exterior parts of the lenticular nucleus, to the optic thalamus, and to the cortex of the parietal lobe. The fibres thus proceeding to the cortex pass through the internal capsule and form the

largest part of the sector of the corona radiata call
tegmental radiations (*Haubenstrahlung*).

The tegmental portion of the **inter-brain** (Art.
subthalamic region, and the gray matter forming t
ventricle and called the interpeduncular region, the
of the posterior perforated lamina (Fig. 247 *Spp*), t
(or mammillaria *Cm*), and the tuber cinereum (*Tc*
region lies between the optic thalamus and the pro
stantia nigra of the crura cerebri, and extends for
perforated lamina (*Lpa*). It is made up of a gray
subthalamicum (Fig. 245 *cs*) or body of Luys, and a
matter connected with the optic thalamus and co
ceeding to the corpus striatum from the red nucle
bellar peduncles.

The **dorsal stratum** of the cerebral axis incl
the corpora quadrigemina, and the thalamus.

The **cerebellum** contains gray matter partly sp
partly collected in the interior in masses known as
nucleus emboliformis, nucleus globosus, and nucl
tively (STILLING). These nuclei are by means of t
matter of the cerebellum connected not only with
(through the several cerebellar peduncles) with vari
already described in the tegmental and peduncul
thus in relation with the cord on the one hand and
mus, lenticular nucleus, and cerebrum on the other

The **quadrigeminal region** consists of two a
terior quadrigeminal bodies enclosing gray nuclei,
which forms the roof or dorsal covering of the aque
posterior bodies are connected by means of the lowe
tral aspect of the tegmental region, and by the inf
the internal geniculate body, a gray nucleus beneat
the optic thalamus. They are probably also in
optic nerves and the cortex cerebri. The anterior
with the optic nerves, with the tegmental region
fillet) and with the cortex cerebri.

The **thalamus** consists of the optic thalamus i
of the term, of the gray matter lining the cavity of
and of the external corpus geniculatum. The opt
tensive connections with the cortex cerebri (these
through the internal capsule, but in part also b
nucleus), with the tegmental region, and also with
outer corpus geniculatum lying towards the outw
pulvinar or posterior tubercle of the thalamus is of
is a centre for the nerves of vision.

The cerebral axis contains no elements subs

function; the **functions** of its centres are partly involuntary or **automatic,** partly **reflex.**

Thus the medulla contains the reflex-centres for closure of the eyelids, for coughing, sneezing, sucking, and so on, together with centres which co-ordinate certain subordinate reflexes within the spinal cord. It also contains the centres which control respiration and the movements of the heart, the vaso-motor centre, and a region which when stimulated gives rise to general convulsions.

Stimulation of the pons causes spasmodic movements and pain; its destruction is followed by paralysis—motor, sensory, and vaso-motor. In the cerebellum and quadrigeminal bodies lie centres for co-ordinating locomotion and other muscular movements.

The functions of the thalamus and of the nuclei of the pons are not certainly known.

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628. The central nervous system is enclosed in three fibrous envelopes or **meninges**—the dura mater, the arachnoid, and the pia mater.

The **dura mater** is a tough vascular membrane traversed by numerous lymphatics. In the cranium it is closely adherent to the bones of the skull: in the vertebral canal it splits into two laminæ, the exterior forming the periosteum of the bony walls, the interior loosely surrounding the cord. Its gives off a fibrous dural sheath to each of the nerves.

The **arachnoid** is a delicate non-vascular membrane everywhere closely applied to the dura mater, with only a capillary space intervening (the subdural space). This interstice is a lymph-space, which communicates with the adjacent lymphatics of the neck, nose, eye, and dura mater, and also with the venous sinuses in the latter (by means of the arachnoidal villi or pacchionian bodies): it is continuous with the subdural spaces within the dural sheaths of the nerves (KEY and RETZIUS), and is everywhere clothed with endothelium.

The **pia mater** is a delicate highly vascular membrane which closely invests the brain and spinal cord. Between the pia mater and the arachnoid lies the subarachnoid space, whose dimensions vary greatly with the varying relations of the two membranes. It is everywhere traversed by delicate fibrous trabeculæ or membranous expansions covered with endothelium (the **subarachnoid tissue**), and contains a liquid known as the cerebrospinal or subarachnoid fluid. The space is narrow over the gyri and wider over the sulci. It is wider still in the spine, and at certain places within the skull where it expands into regular sinuses or **cisterns.** Such for example occur between the dorsal surface of the medulla and the posterior part of the cerebellum, in the interpeduncular space (between the crura cerebri), in front of the optic chiasma, between the under surface of the cerebellar hemispheres and the lateral portions of the medulla, on both sides of the transverse fissure, and at the lower ends of the sylvian fissures.

The pia mater and subarachnoid tissue send processes into the cleft between the cerebellum and medulla, and into that between the upper surface of the cerebellum and corpora quadrigemina and the under surface of the cerebrum: these processes are continued into the interior of the adjoining ventricles and form the telæ choroideæ and **choroid plexuses.** Here also are the chief channels of communication between the subarachnoid cisterns and the cavities of the fourth (foramen of Magendie) and third ventricles.

The subarachnoid spaces thus communicate not only with each other but also with the cerebral ventricles. The spaces also communicate with the lymphatics of the head, with the lymph-spaces of the nerves as they take their exit, and with the dural venous sinuses. Communication with the lymphatics of the neck and of the nerves takes place by means of the pia mater (**pial sheaths**) which surround the vessels and nerves as they enter or leave. With the dural sinuses communication takes place by means of the pacchionian bodies, which are rounded excrescences of arachnoid and subarachnoid tissue penetrating into the dura, and separated only by a thin dural film from the venous blood in the sinuses.

The cerebral **blood-vessels** before they enter the brain all pass through the subarachnoid space and the pia mater, and carry with them a pial sheath. They are thus even within the brain surrounded by lymph-spaces, which are known as adventitial **lymph-sheaths** (VIRCHOW, ROBIN) and communicate freely with the pial spaces. The central nervous system is thus not only surrounded on all sides by lymph-spaces but also traversed in all directions by lymph-channels, and its blood-vessels all lie in lymph-sheaths.

The arteries of the brain are divided into basal or ganglionic and cortical (HEUBNER, DURET). The former are terminal arteries, ramifying in the basal ganglia and the internal capsule; the latter anastomose

freely within the pia mater. The choroid plexuses also carry vessels into the interior of the ventricles; they may be described as villous processes covered with polygonal epithelium and containing a multitude of capillary loops of large size.

The vessels of the cord pass into the nerve-substance partly from the periphery, partly by way of the longitudinal fissures.

Many authors (such as HIS, ROTH, etc.) affirm that circumvascular and epicerebral lymph-spaces exist outside the adventitia of the vessels and beneath the pia mater, and that these spaces are traversed by fine trabecula emerging from the brain-substance and passing into the adventitia of the vessels. ZIEGLER, with BOLL, GOLGI, and others, makes out that these spaces, when they are met with at all, are due to artificial causes such as the hardening of the brain in solutions of chromic acid and so on.

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629. The central nervous system is composed of tissue the normal performance of whose functions depends greatly on the normal circulation of healthy blood within it.

A brief obstruction to the inflow or outflow of blood is sufficient to give rise to grave disorder of the nervous functions, and in like manner an excess of carbonic acid or a deficiency of oxygen may give rise to serious irritation or paralysis of particular parts. When such disturbances of circulation or nutrition reach a certain degree of gravity they are apt to be followed by transient or permanent degenerative changes in the nervous structures. Such **degenerations** form the basis of an important group of diseases of the brain and cord.

In many acute febrile disorders disturbance of the cerebral functions is a symptom. This disturbance is due partly to over-heating of the tissues, partly to disorder of the circulation, partly to impurities and changes in the composition of the blood. The fact that permanent lesions of the brain and cord are comparatively rare sequelæ of such fevers shows that nerve-substance has a remarkable power of resistance to a number of injurious agencies, that in other words the brain and

cord like other organs can be permanently injured only by agencies of particular kinds. That these agencies have about them something special is made likely by the fact—that many **poisons** when introduced into the blood exert a marked specific action on the nerve-cells and nerve-fibres, while others have no action whatever on these structures.

Every-day experience shows that personal **predisposition** plays an unusually important part in the genesis of central nervous diseases. This predisposition is usually inherited, seldom acquired. According to WESTPHAL in 50 per cent of insane patients the occurrence of disease of the central nervous system in some blood-relation of the ascending line can be demonstrated. It is not actual disease which is thus transmitted from parent to child but only a liability to disease, a lack of resisting-power, in consequence of which influences (unable in a normal individual to produce any abiding disturbance) are capable of setting up disorders of function and often alterations of structure. The morbid influences may be of any kind, and may reach the central nervous system either by way of the circulation or as morbid stimuli by way of the nerves.

Predisposition to nervous disease is usually a matter beyond the scope of anatomical research, but cases do occur in which the inherited or at least congenital pathological condition manifests itself as a defect of development in the central nervous system. In other words **malformations** of the brain are very commonly associated with defective brain-function, and constitute a predisposition to further nervous disease.

Inherited and acquired predisposition is of special importance in connection with diseases of the central nervous system that are chronic. It has little to do with the genesis of acute and particularly of inflammatory disorders, which are as a rule set up by irritant matters reaching the nerve-tissues through the **circulation.**

A common source of brain-affections, especially of the inflammatory kind, is disease of the adjacent structures, such as the base of the skull, the petrous bone, the skull-cap, the nose and its cavities, etc. The contents of the cranium and vertebral canal are in communication by means of blood-vessels and lymphatics with the surrounding parts, and thus inflammatory mischief may invade the brain and cord not only by **direct extension** but also through the blood and lymph.

Lastly, both brain and cord are much exposed to injury by **traumatic violence** of the most various kinds, and in consequence undergo a great variety of morbid changes which are often extremely grave.

CHAPTER XCII.

MALFORMATIONS OF THE BRAIN AND SPINAL CORD.

630. The cerebrospinal system takes its origin from the **medullary tube** or canal formed by the infolding of the epiblast along the medullary groove. The cells lining the lumen of this tube become the ciliated epithelium of the central canal and ventricles of the cord and brain, the remaining cells develop into the ganglion-cells and their processes.

The rudiment of the brain appears as three primary **cerebral vesicles,** which are simply dilatations of the anterior end of the medullary tube. The first and third vesicles each divide into two, and thus five vesicles are produced from whose walls the various parts of the brain are developed. From the first vesicle (**fore-brain** or prosencephalon) are formed the cerebral hemispheres, the corpora striata, the lenticular nucleus, the corpus callosum, and the fornix: from the others, which are known as the **inter-brain** (thalamencephalon), **mid-brain** (mesencephalon), **hind-brain** (epencephalon), and **after-brain** (metencephalon), are derived the various parts of the cerebral axis and its dorsal stratum.

In the region of the after-brain (or medulla oblongata) the medullary tube never completely closes, so that here a communication with the interior of the tube remains open. The development of the fore-brain proceeds rapidly, and the cerebral hemispheres thus produced in the human adult ultimately overlie almost all the rest of the brain.

If the formation of the medullary tube from the medullary groove of the embryo is for any reason interfered with, or if the dorsal wall of the tube is imperfectly formed or destroyed, the cerebrum and part of the cerebral axis remain undeveloped, and we have the condition known as **total anencephalia.** According to LEBEDEFF the same result may take place if the cranial flexure of the embryo be abnormally sharp. G. ST. HILAIRE, FÖRSTER, and PANUM think that the absence of the brain is chiefly owing to an excessive accumulation of liquid in the medullary tube. DARESTE and PERLS on the other hand are of opinion that anencephalia is due to an abnormal pressure of the head-fold of the amnion on the cephalic end the embryo (Art. 7). When for any reason some part of the medullary tube is destroyed or hindered in its development the growth of the lateral medullary plates does not entirely cease (LEBEDEFF); they enlarge and form a number of folds buried in the

course longitudinally for a short distance along the cord before entering the gray horns.

The median portion of each **posterior column** is called the **column of Goll** or *funiculus gracilis* (*fgr*); the lateral portion (*fcn*) is the **column of Burdach** or cuneate funiculus. The column of Goll connects the posterior roots of the cord with the tegmental region of the medulla, *i. e.* with the nucleus of the funiculus gracilis (Fig. 249 *ng*), probably also with the internal accessory olivary nucleus (*oam*), and thence by way of the internal capsule and the corona radiata with the parietal zone of the cortex and the lenticular nucleus. The column of Burdach (Fig. 243 *fcn*) contains fibres which enter with the posterior roots and then pass upwards for a certain distance, ultimately entering the posterior horn. It also contains fibres interconnecting various portions of gray matter in the cord, and connecting these with the nucleus of the funiculus cuneatus and olivary body in the medulla, with the dentate nucleus in the cerebellum, and thence with the parietal zone of the cortex and the corpus striatum (FLECHSIG). According to KAHLER the ascending nerve-fibres from the posterior roots are so arranged that in any given section of the cord those fibres which entered lowest lie nearest the posterior end of the median fissure.

The gray matter of the cord contains the several nerve centres subordinate to those in the medulla; these centres subserve simple or partial and diffuse or co-ordinated reflexes, and on stimulation of the sensory or afferent fibres may give rise to motor impulses which act on associated or distinct groups of muscles and result in motions of a complicated kind. Such are the centres for defæcation, for micturition, for erection and ejaculation, and for various vaso-motor actions.

The fibres connecting the cord with the brain subserve the perception of sensations, and the transmission of impulses inhibiting reflex actions and calling forth voluntary movements.

On the structure and functions of the cord:—TÜRCK, *Wiener Sitzungsberichte* 1851, 1853, 1855; VAN DER KOLK, *Structure and functions of the spinal cord* (New Syd. Soc.) London 1859; GOLL, *Denkschr. d. med. chir. Gesellsch. d. Cant. Zürich* 1860; DEITERS, *Untersuch. üb. Gehirn u. Rückenmark* 1865; BOUCHARD, *Archives gén.* 1866; M. SCHULTZE, *Stricker's Manual of Histology* (New Syd. Soc.) II. London 1872; GERLACH, *ibid.*; LEYDEN, *Klinik d. Rückenmarkskrankh.* Berlin 1874; HUGUENIN, *Allg. Path. d. Krankh. d. Nervensyst.* Zürich 1873; BOLL, *Histol. d. nerv. Centralorg.*, *Arch. f. Psych.* IV.; SCHIEFFERDECKER, *Beiträge z. Kenntniss d. Faserverlaufes im Rückenmark*, *Arch. f. mikros. Anat.* X. (1874), *Virch. Arch.* vol. 67; EICHHORST, *ibid.* vol. 64; FLECHSIG, *Die Leitungsbahnen im Gehirn u. Rückenmark* Leipzig 1876, *Arch. d. Heilk.* XVIII., XIX., *Ziemssen's Cyclop.* (supp. vol.); ERB, *Ziemssen's Cyclop.* XIII.; KLEIN and NOBLE SMITH, *Atlas of Histology* London 1880; CHARCOT, *Diseases of the nervous system* (New Syd. Soc.) London 1876–80, *Localization of cerebral and spinal diseases* (New Syd. Soc.) London 1883; SINGER, *Wiener Sitzungsberichte* 1881; DEBOVE and GOMBAULT, *Arch. de neurologie* I. (1881); SCHWALBE, *Lehrb. d. Neurologie* Erlangen 1881; ROSS, *Diseases of the nervous system* I. London 1883;

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627. The **cerebral axis** consists of the medulla oblongata (Fig. 247 *Mobl*), the pons Varolii (*Po*), the crura cerebri (*Pe*), the subthalamic (or interpeduncular) region (Fig. 245 about *cs*) with the tuber cinereum (Fig. 247 *Tc*), corpora albicantia (or mammillaria *Cm*), the cerebellum (*D*, *Gr*, *Fl*), the corpora quadrigemina (Fig. 248 *h*), and the optic thalamus (Fig. 245 *th*).

Genetically all these are but modified parts of the spinal cord

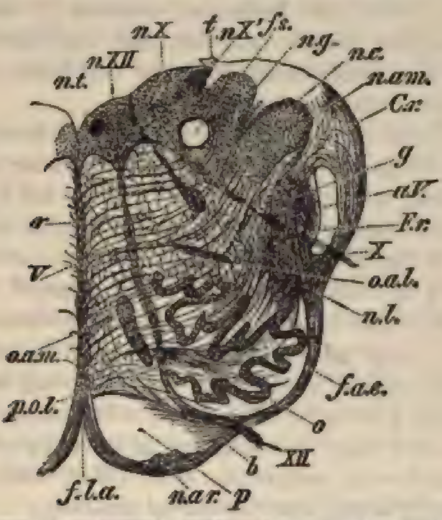

FIG. 249. SECTION OF THE MEDULLA THROUGH THE MIDDLE OF THE OLIVARY BODY.
(*After SCHWALBE*: × 4.)

nt, nucleus of the funiculus teres
nXII, nucles of the hypoglossal nerve
*nX nX*₁, nucleus of the vagus nerve
XII, hypoglossal nerve
X, vagus nerve
o, olivary nucleus (*corpus dentatum*)
oal, exterior accessory olivary nucleus
oam, interior accessory olivary nucleus
nam, nucleus ambiguus
nl, nucleus of lateral column
ng, nucleus of funiculus gracilis
nc, nucleus of funiculus cuneatus
nar, nucleus arciformis
g, substantia gelatinosa
aV, ascending root of trigeminus
fs, funiculus solitarius
t, origin of the *ligula* (tænia sinus rhomboidalis)
Cr, restiform body
p, pyramid
fae, external arciform fibres passing in part through the substantia gelatinosa (*g*), in part external to the restiform body (*Cr*)
Fr, formatio reticularis, showing internal arciform fibres; the latter partly continuous with the external arciform fibres, partly arising from the various gray nuclei and passing towards the raphe (*r*)
pol, olivary arciform fibres (*pedunculus olivæ*)
V, continuation of anterior column of cord
fla, anterior median fissure

(SCHWALBE), and from this region arise those cranial nerves which are homologous with the spinal nerves.

The modifications which the cord undergoes in this region are chiefly these—the central canal becomes more and more posterior and is continued into the cerebral axis as the fourth ventricle, the aqueduct of Sylvius, and the third ventricle. At the same time the gray matter subdivides, and interpenetrating the white assumes a peculiar reticulated structure (Fig. 249 *Fr*) with numerous detached clusters of ganglion-cells from which the cranial nerves take their origin (Fig. 248).

This subdivision of the gray matter is accompanied by certain rearrangements of the nerve-tracts. The pyramidal lateral columns cross each other at the decussation (Fig. 247 *DPy*), and pass to the ventral surface of the medulla (Fig. 248 *p*), while the shorter tracts connecting the several portions of the gray matter become less and less superficial. The column of Goll and the column of Burdach pass up (as the funiculus gracilis (Fig. 248 *a*) and funiculus cuneatus (*b*) respectively) to the lateral margin of the fourth ventricle, and together with lateral cerebellar tract and the arciform fibres of the restiform body (*c*) form the posterior peduncle of the cerebellum (*e*).

At this level fresh nuclei begin to appear, and form the substance of the olivary body (Figs. 247, 249 *o*), and the beginning of the gray matter of the cerebellum, corpora quadrigemina (Fig. 248 *h*), optic thalamus (Fig. 245 *th*), subthalamic body (*cs*), and numerous small masses (Fig. 249) embedded in the various columns and tracts. All these nuclei give rise in their turn to fresh bundles of fibres, some of which run in distinct tracts while others interlace with their neighbors.

Presently the longitudinal fibres are crossed by numerous arciform fibres (Fig. 249) some external (*fae*), others lying deeper (*Fr*, *b*) and forming a network (*formatio reticularis*) with the longitudinal fibres.

The cerebral axis may be considered as made up of three regions or strata (SCHWALBE)—the peduncular tract (MEYNERT, SCHWALBE), the tegmental region (FOREL), and the dorsal stratum.

The **peduncular tract** is in the **medulla** represented by the pyramidal columns (Fig. 249 *p*), which are surrounded and in part reinforced by the external arciform fibres (*fae*). The external arciform fibres enclose a nucleus known as the arciform nucleus (*nar*). In the **pons** the peduncular tract lies in the ventral stratum, being crossed and interlaced by the transverse arciform fibres derived from the middle peduncle of the cerebellum (Fig. 247 *BrS*). Some of these fibres are commissural and connect the two halves of the cerebellum; others penetrate the gray masses embedded among the arciform fibres and known as the nuclei of the pons. Certain of the nerve fibres which start from these nuclei join the bundles of pyramidal fibres and pass with them up to the cerebrum.

The bundles of pyramidal fibres, which in the pons are more or less subdivided and scattered, unite again into compact bundles on the anterior or cerebral side of the pons and, reinforced by the nuclear fibres

just referred to, form the pes or crusta of the **crura cerebri** (Fig. 247 *Pe*). The crusta is covered on the upper or dorsal surface by the substantia nigra, a layer of pigmented ganglion-cells, which in their turn give off fibres to join the crustal fibres. These latter then pass (mainly through the internal capsule) up to the cortex. The pyramidal fibres terminate in the ascending frontal and parietal convolutions and the parts adjoining, the other fibres pass to the frontal, temporal, and occipital lobes. A few enter the lenticular and caudate nuclei.

The **tegmental region** lies to the dorsal surface of the peduncular tract, and consists chiefly of the formatio reticularis (Fig. 249 *Fr*). The reticular structure is due to the subdivision into fibres of part of the gray matter of the anterior horn, with which are interlaced numerous arciform fibres. It includes in every part longitudinal fibres which are the continuation of the anterior and lateral columns of the cord, together with arciform fibres and scattered ganglion-cells. Posteriorly there is a so-called raphe (*r*), due to the decussation of some of the fibres in the middle line.

The tegmental portion of the **medulla** contains the nuclei of the twelfth, eleventh, tenth, ninth, and part of the eighth cranial nerves (Figs. 248, 249), the olivary nucleus (Fig. 249 *o*), the accessory olivary nuclei (*oam, oal*), the nucleus of the funiculus gracilis (*ng*), the nucleus of the funiculus cuneatus (*nc*), and other nuclei. The restiform body (Fig. 248 *c*) also belongs to this region, through which pass fibres from the lateral cerebellar tract of the cord, from the olivary body, and from the formatio reticularis, to the cerebellum.

The tegmental portion of the **pons** contains the nuclei of the fifth, sixth, seventh, and part of the eighth cranial nerves (Fig. 248). Fibres pass from the cerebellum into the formatio reticularis through the anterior peduncle of the cerebellum.

The tegmental portion of the **crura cerebri** lies beneath the aqueduct of Sylvius and is connected with the corpora quadrigemina and the anterior medullary velum. Beneath the aqueduct lies the nucleus of the third and fourth cranial nerves (Fig. 248). The formatio reticularis which lies to the ventral side of these nuclei contains (in addition to longitudinal bundles of fibres from the anterior and lateral columns of the cord) fibres from the corpora quadrigemina and anterior medullary velum, and from the cerebellum. The former proceed to the pons by way of the arcuate fibres, the latter by way of the anterior peduncles. The bundles from the cerebellum enclose in the part beneath the anterior corpora quadrigemina a reddish island of gray matter known as the red nucleus. Many of the fibres of these bundles terminate in this nucleus (GUDDEN), a few are seen to pass beyond it (FLECHSIG). These latter fibres pass to the exterior parts of the lenticular nucleus, to the optic thalamus, and to the cortex of the parietal lobe. The fibres thus proceeding to the cortex pass through the internal capsule and form the

largest part of the sector of the corona radiata called by FLECHSIG the tegmental radiations (*Haubenstrahlung*).

The tegmental portion of the **inter-brain** (Art. 630) consists of the subthalamic region, and the gray matter forming the floor of the third ventricle and called the interpeduncular region, the latter being made up of the posterior perforated lamina (Fig. 247 *Spp*), the corpora albicantia (or mammillaria *Cm*), and the tuber cinereum (*Tc*). The subthalamic region lies between the optic thalamus and the prolongation of the substantia nigra of the crura cerebri, and extends forwards to the anterior perforated lamina (*Lpa*). It is made up of a gray nucleus, the corpus subthalamicum (Fig. 245 *cs*) or body of Luys, and a dorsal layer of white matter connected with the optic thalamus and containing fibres proceeding to the corpus striatum from the red nucleus and superior cerebellar peduncles.

The **dorsal stratum** of the cerebral axis includes the cerebellum, the corpora quadrigemina, and the thalamus.

The **cerebellum** contains gray matter partly spread over the cortex, partly collected in the interior in masses known as the nucleus dentatus, nucleus emboliformis, nucleus globosus, and nucleus fastigii, respectively (STILLING). These nuclei are by means of the fibres of the white matter of the cerebellum connected not only with each other, but also (through the several cerebellar peduncles) with various nuclei and tracts already described in the tegmental and peduncular regions; they are thus in relation with the cord on the one hand and with the optic thalamus, lenticular nucleus, and cerebrum on the other.

The **quadrigeminal region** consists of two anterior and two posterior quadrigeminal bodies enclosing gray nuclei, and the gray lamina which forms the roof or dorsal covering of the aqueduct of Sylvius. The posterior bodies are connected by means of the lower fillet with the ventral aspect of the tegmental region, and by the inferior brachium with the internal geniculate body, a gray nucleus beneath and contiguous to the optic thalamus. They are probably also in connection with the optic nerves and the cortex cerebri. The anterior bodies are connected with the optic nerves, with the tegmental region (through the upper fillet) and with the cortex cerebri.

The **thalamus** consists of the optic thalamus in the narrower sense of the term, of the gray matter lining the cavity of the third ventricle, and of the external corpus geniculatum. The optic thalamus has extensive connections with the cortex cerebri (these pass outwards chiefly through the internal capsule, but in part also beneath the lenticular nucleus), with the tegmental region, and also with the optic tract. The outer corpus geniculatum lying towards the outward extremity of the pulvinar or posterior tubercle of the thalamus is of a dark-gray tint; it is a centre for the nerves of vision.

The cerebral axis contains no elements subserving any psychical

function; the **functions** of its centres are partly involuntary or **automatic**, partly **reflex.**

Thus the medulla contains the reflex-centres for closure of the eyelids, for coughing, sneezing, sucking, and so on, together with centres which co-ordinate certain subordinate reflexes within the spinal cord. It also contains the centres which control respiration and the movements of the heart, the vaso-motor centre, and a region which when stimulated gives rise to general convulsions.

Stimulation of the pons causes spasmodic movements and pain; its destruction is followed by paralysis—motor, sensory, and vaso-motor. In the cerebellum and quadrigeminal bodies lie centres for co-ordinating locomotion and other muscular movements.

The functions of the thalamus and of the nuclei of the pons are not certainly known.

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628. The central nervous system is enclosed in three fibrous envelopes or **meninges**—the dura mater, the arachnoid, and the pia mater.

The **dura mater** is a tough vascular membrane traversed by numerous lymphatics. In the cranium it is closely adherent to the bones of the skull: in the vertebral canal it splits into two laminæ, the exterior forming the periosteum of the bony walls, the interior loosely surrounding the cord. Its gives off a fibrous dural sheath to each of the nerves.

The **arachnoid** is a delicate non-vascular membrane everywhere closely applied to the dura mater, with only a capillary space intervening (the subdural space). This interstice is a lymph-space, which communicates with the adjacent lymphatics of the neck, nose, eye, and dura mater, and also with the venous sinuses in the latter (by means of the arachnoidal villi or pacchionian bodies): it is continuous with the subdural spaces within the dural sheaths of the nerves (KEY and RETZIUS), and is everywhere clothed with endothelium.

The **pia mater** is a delicate highly vascular me invests the brain and spinal cord. Between th arachnoid lies the subarachnoid space, whose dim with the varying relations of the two membrane traversed by delicate fibrous trabeculæ or membra ered with endothelium (the **subarachnoid tissue**). known as the cerebrospinal or subarachnoid fluid. over the gyri and wider over the sulci. It is wider at certain places within the skull where it expands i **cisterns.** Such for example occur between the d medulla and the posterior part of the cerebellum, in space (between the crura cerebri), in front of th tween the under surface of the cerebellar hemisph portions of the medulla, on both sides of the tran the lower ends of the sylvian fissures.

The pia mater and subarachnoid tissue send pr between the cerebellum and medulla, and into that surface of the cerebellum and corpora quadrigemina face of the cerebrum: these processes are continued the adjoining ventricles and form the telæ cho **plexuses.** Here also are the chief channels of com the subarachnoid cisterns and the cavities of the Magendie) and third ventricles.

The subarachnoid spaces thus communicate not but also with the cerebral ventricles. The spac with the lymphatics of the head, with the lymph-sp they take their exit, and with the dural venous si tion with the lymphatics of the neck and of the n means of the pia mater (**pial sheaths**) which surro nerves as they enter or leave. With the dural sin takes place by means of the pacchionian bodies, wh crescences of arachnoid and subarachnoid tissue p dura, and separated only by a thin dural film from the sinuses.

The cerebral **blood-vessels** before they enter through the subarachnoid space and the pia mater, a pial sheath. They are thus even within the b lymph-spaces, which are known as adventitial **lym** CHOW, ROBIN) and communicate freely with the pi tral nervous system is thus not only surrounded on spaces but also traversed in all directions by lymp blood-vessels all lie in lymph-sheaths.

The arteries of the brain are divided into basal or tical (HEUBNER, DURET). The former are terminal in the basal ganglia and the internal capsule; th

freely within the pia mater. The choroid plexuses also carry vessels into the interior of the ventricles; they may be described as villous processes covered with polygonal epithelium and containing a multitude of capillary loops of large size.

The vessels of the cord pass into the nerve-substance partly from the periphery, partly by way of the longitudinal fissures.

Many authors (such as HIS, ROTH, etc.) affirm that circumvascular and epicerebral lymph-spaces exist outside the adventitia of the vessels and beneath the pia mater, and that these spaces are traversed by fine trabecula emerging from the brain-substance and passing into the adventitia of the vessels. ZIEGLER, with BOLL, GOLGI, and others, makes out that these spaces, when they are met with at all, are due to artificial causes such as the hardening of the brain in solutions of chromic acid and so on.

References on the membranes and vessels of the brain and cord:—HIS, *Zeitschrift f. wissenschaft. Zool.* XV. (1864); ROBIN, *Journ. de physiol.* II. (1859); ROTH, *Virch. Arch.* vol. 46; AXEL KEY and G. RETZIUS, *Studien in d. Anatomie d. Nervensystemes u. d. Bindegewebes* I. and II. Stockholm 1875–76; SCHWALBE, *Med. Centralb.* 30, 1869, *Arch. f. mikrosk. Anat.* VI (1870), *Lehrb. d. Neurol.* 1881; SÉE, *Revue mensuelle* II. (1878); RIEDEL, *Arch. f. mikrosk. Anat.* XI. (1875); OBERSTEINER, *Wiener Sitzungsber.* LXI. (1870); GOLGI, *Rivista clinica* Nov. 1871; BOLL, *Arch. f. Psych.* IV. (1873); LÖWE, *ibid.* VII.; HEUBNER, *Cent. f. med. Wiss.* 1872, *Die luetische Erkrankung d. Hirnarterien* Leipzig 1874; DURET, *Recherches anatomiques sur la circulation de l'encéphale, Arch. de physiol.* 1874; ADAMKIEWICZ, *Die Blutgefässe d. menschlichen Rückenmarkes, Wiener Sitzungsber.* LXXXIV., LXXXV. (1881–82), *Trans. internat. med. Congress* I. London 1881; MOSSO, *Ueber d. Kreislauf d. Blutes im menschlichen Gehirn* Leipzig 1881; CHARCOT, *Leçons sur les localisations* Paris 1876, trans. by HADDEN (New Syd. Soc.) London 1883; KLEIN and NOBLE SMITH, *Atlas of Histology* London 1880; ROSS, *Brain* III. (1880), *Diseases of the nervous system* London 1883.

629. The central nervous system is composed of tissue the normal performance of whose functions depends greatly on the normal circulation of healthy blood within it.

A brief obstruction to the inflow or outflow of blood is sufficient to give rise to grave disorder of the nervous functions, and in like manner an excess of carbonic acid or a deficiency of oxygen may give rise to serious irritation or paralysis of particular parts. When such disturbances of circulation or nutrition reach a certain degree of gravity they are apt to be followed by transient or permanent degenerative changes in the nervous structures. Such **degenerations** form the basis of an important group of diseases of the brain and cord.

In many acute febrile disorders disturbance of the cerebral functions is a symptom. This disturbance is due partly to over-heating of the tissues, partly to disorder of the circulation, partly to impurities and changes in the composition of the blood. The fact that permanent lesions of the brain and cord are comparatively rare sequelæ of such fevers shows that nerve-substance has a remarkable power of resistance to a number of injurious agencies, that in other words the brain and

cord like other organs can be permanently injured only by agencies of particular kinds. That these agencies have about them something special is made likely by the fact—that many **poisons** when introduced into the blood exert a marked specific action on the nerve-cells and nerve-fibres, while others have no action whatever on these structures.

Every-day experience shows that personal **predisposition** plays an unusually important part in the genesis of central nervous diseases. This predisposition is usually inherited, seldom acquired. According to WESTPHAL in 50 per cent of insane patients the occurrence of disease of the central nervous system in some blood-relation of the ascending line can be demonstrated. It is not actual disease which is thus transmitted from parent to child but only a liability to disease, a lack of resisting-power, in consequence of which influences (unable in a normal individual to produce any abiding disturbance) are capable of setting up disorders of function and often alterations of structure. The morbid influences may be of any kind, and may reach the central nervous system either by way of the circulation or as morbid stimuli by way of the nerves.

Predisposition to nervous disease is usually a matter beyond the scope of anatomical research, but cases do occur in which the inherited or at least congenital pathological condition manifests itself as a defect of development in the central nervous system. In other words **malformations** of the brain are very commonly associated with defective brain-function, and constitute a predisposition to further nervous disease.

Inherited and acquired predisposition is of special importance in connection with diseases of the central nervous system that are chronic. It has little to do with the genesis of acute and particularly of inflammatory disorders, which are as a rule set up by irritant matters reaching the nerve-tissues through the **circulation.**

A common source of brain-affections, especially of the inflammatory kind, is disease of the adjacent structures, such as the base of the skull, the petrous bone, the skull-cap, the nose and its cavities, etc. The contents of the cranium and vertebral canal are in communication by means of blood-vessels and lymphatics with the surrounding parts, and thus inflammatory mischief may invade the brain and cord not only by **direct extension** but also through the blood and lymph.

Lastly, both brain and cord are much exposed to injury by **traumatic violence** of the most various kinds, and in consequence undergo a great variety of morbid changes which are often extremely grave.

CHAPTER XCII.

MALFORMATIONS OF THE BRAIN AND SPINAL CORD.

630. The cerebrospinal system takes its origin from the **medullary tube** or canal formed by the infolding of the epiblast along the medullary groove. The cells lining the lumen of this tube become the ciliated epithelium of the central canal and ventricles of the cord and brain, the remaining cells develop into the ganglion-cells and their processes.

The rudiment of the brain appears as three primary **cerebral vesicles,** which are simply dilatations of the anterior end of the medullary tube. The first and third vesicles each divide into two, and thus five vesicles are produced from whose walls the various parts of the brain are developed. From the first vesicle (**fore-brain** or prosencephalon) are formed the cerebral hemispheres, the corpora striata, the lenticular nucleus, the corpus callosum, and the fornix: from the others, which are known as the **inter-brain** (thalamencephalon), **mid-brain** (mesencephalon), **hind-brain** (epencephalon), and **after-brain** (metencephalon), are derived the various parts of the cerebral axis and its dorsal stratum.

In the region of the after-brain (or medulla oblongata) the medullary tube never completely closes, so that here a communication with the interior of the tube remains open. The development of the fore-brain proceeds rapidly, and the cerebral hemispheres thus produced in the human adult ultimately overlie almost all the rest of the brain.

If the formation of the medullary tube from the medullary groove of the embryo is for any reason interfered with, or if the dorsal wall of the tube is imperfectly formed or destroyed, the cerebrum and part of the cerebral axis remain undeveloped, and we have the condition known as **total anencephalia.** According to LEBEDEFF the same result may take place if the cranial flexure of the embryo be abnormally sharp. G. ST. HILAIRE, FÖRSTER, and PANUM think that the absence of the brain is chiefly owing to an excessive accumulation of liquid in the medullary tube. DARESTE and PERLS on the other hand are of opinion that anencephalia is due to an abnormal pressure of the head-fold of the amnion on the cephalic end the embryo (Art. 7). When for any reason some part of the medullary tube is destroyed or hindered in its development the growth of the lateral medullary plates does not entirely cease (LEBEDEFF); they enlarge and form a number of folds buried in the

substance of the mesoblast, and becoming partially abstricted take the form of irregular cysts and cavities. When the liquor amnii makes its appearance the exposed medullary plates are usually much damaged; the underlying mesoblast develops at the same time into the cerebral membranes, and the result is that instead of a brain we have covering the base of the skull a mass of vascular connective tissue containing cystic cavities and marrow-like remnants of brain-substance. As the dorsal wall of the medullary tube was defective or absent, the cranial vault is more or less defective or absent, and the anencephalia is thus associated with conditions known as **acrania, hemicephalus,** or **cranioschisis** (Art. 7).

When the development of the brain is only in part interfered with, or when parts only of the rudimental structures have been destroyed in an early stage, the result is some partial deficiency which we may appropriately call **partial anencephalia.**

The situation, size, and extent of such deficiencies may of course vary greatly in different cases, and give rise to a great variety of brain-deformities. If the skull is closed (and in these cases it usually is closed) the space left vacant by the ill-developed brain becomes filled with liquid, which gathers either in the subarachnoid tissue outside the existing brain-mass, or within it in one of its ventricles, or in both places together. The latter forms have been described by CRUVEILHIER as hydrocephalic anencephalia.

Cases of anencephalia also occur in which more or less important parts of the base of the brain (*e. g.* the basal ganglia) are properly developed, and others in which while one hemisphere is developed (though perhaps malformed) the other hemisphere is wanting. The cranial vault in such cases may either be entire, defective, or distended as in hydrocephalus (Art. 631). When the vault is closed the fragments of brain-substance are shut off from the space filled with liquid by a fibrous partition representing some of the cerebral membranes. If the defect of development has mainly affected the anterior part of the fore-brain we have the malformation known as **synophthalmia** or **cyclopia,** and **arhinencephalia** (KUNDRAT). In the latter form the nose is undeveloped, in the former the eyes (Art. 7). The nose sometimes takes the form of a snout-like projection (ethmocephalia), sometimes it is a mere stunted remnant (cebocephalia); in other cases again there is a median fissure of the upper lip and of the septum of the nose, or a single or double lateral hare-lip and cleft-palate. In the slightest variety of the malformation the face is normal, the brow alone being narrow and tapering.

In both synophthalmia and arhinencephalia the cerebrum is more or less malformed: in the gravest variety the brain is represented by a mere pointed vesicle. In slighter cases particular parts are wanting, such as the olfactory nerve and lobe, the corpus callosum, some of the convolu-

tions, etc. The quadrigeminal bodies are often coalescent. The optic chiasma and tracts are sometimes absent, sometimes normal.

Between such grave defects and the slightest, involving perhaps merely a portion of one convolution, all intermediate varieties of malformation are met with.

The slightest kind of defect occurring on the outer surface of the brain takes the form of shallow depressions or excavations of the gyri, the hollows being lined with pia mater. When entire gyri or considerable portions of gyri are wanting the defects appear as open clefts or funnel-shaped pits or perforations extending sometimes to the walls or even into the interior of the ventricles. This condition has been called **porencephalia** (HENSCHL). The cavities are lined with pia mater, which is discontinuous only where they commmunicate with the cavity of the ventricle. The spaces thus formed are in general filled up with liquid collected in the subarachnoid tissue, and are bridged over and enclosed by the arachnoid membrane. In other cases the adjacent convolutions are pressed together over the gap, which then takes the form of a deep cleft or interstice.

When the defect is larger (involving it may be a lobe or more) similar conditions obtain. The neighboring ventricles are seldom of normal size, being usually more or less dilated or showing local sacculations opposite to the missing regions. The surrounding convolutions tend to be arranged radially round the gap as if puckered and drawn into it. The remainder of the brain may be quite normal, but at times the convolutions are abnormally arranged or ill-developed. The basal ganglia on the side of the dilated ventricles are flattened. The cranium is either normal or somewhat asymmetrical. When the brain is imperfect the skull is usually small, but in marked ventricular hydrocephalus it is enlarged.

Another variety of partial anencephalia is the absence of some of the deeper structures and especially of the basal ganglia. Thus the corpus callosum and fornix may be wanting or imperfect, and so likewise may the gray commissure of the third ventricle, the corpora albicantia, the corpora quadrigemina, etc. When the corpus callosum is absent the gyrus fornicatus and gyrus hippocampi are usually absent also, and some of the other convolutions are frequently irregular in form or arrangement.

The causation of partial anencephalia is not the same in all cases. Porencephalia is probably in many cases due to intra-uterine disorders of circulation, hæmorrhages, and inflammations, by which portions of the brain already developed are damaged or destroyed. In favor of this view is the fact—that the brain-substance and the membranes in the neighborhood of the defect often show changes similar to those which in later life are known to follow upon submeningeal anæmic and inflammatory softening (Art. 642). Pressure from without or a blow on the cranium may in some cases bring about a like result.

In others internal or ventricular hydrocephalus (Art. 631) may disturb the circulation of the part and lead to its wasting or disappearance. When the convolutions about the defect are normal it is probable that the destruction took place at a time when the brain was fairly developed, say not later than the fifth month. Obvious disturbance of the configuration of the brain would imply an earlier date. Occasionally such local defects must be due to actual failure of development, or **agenesis** as it might be called. Deficiencies in the deeper parts of the brain are usually unaccompanied by any signs of destructive disease; they would therefore seem to be due to primary failure of development.

The condition of the cord corresponding to anencephalia is called **amyelia.** Most frequently the two go together, and are accompanied by defects of the vertebral arches and of the meninges and integuments. A cleft thus extends from the opening in the cranium down to the cervical, dorsal, or it may be to the sacral region (**rhachischisis**). Clefts of the dorsal or lumbar spine alone, extending through the skin, are more rare. Where the vertebral arches are absent the cord is also wanting, so that the vertebral bodies are covered only by membranes. Such defects are due either to some sharp flexure of the embryo, to imperfect separation of the medullary plate from the superficial or epidermic epiblast, or to dropsical distention of the medullary tube. Partial defects of the cord are very rare when the spinal canal is closed. On the other hand ADAMKIEWICZ states that in 80 persons out of 100 some of the 31 pairs of roots of the spinal nerves will exhibit more or less marked defects, especially in the anterior roots. Slight asymmetry of the cord, chiefly in the decussation of the pyramids in the medulla, is an extremely common phenomenon.

The term **porencephalia** (or porencephalus) is used in different senses by different writers, some confining it to congenital defects, others applying it to those which are acquired after birth. Many apply it only to small and localised defects, others extend it so that it might imply the absence of an entire cerebral hemisphere. It seems better to limit its application to localized defects that are congenital or at least acquired in early infancy.

When in total or partial anencephalia the motor centres and tracts are wanting, the pyramidal tracts and columns of the cord do not develop (FLECHSIG). And in partial failure of development (agenesis) of the brain FICK observes that the pyramidal tracts are imperfectly differentiated, the medullary sheath of the fibres being ill-developed.

References on anencephalia and amyelia:—DARESTE, *Recherches sur la production des monstruosités* Paris 1877; PERLS, *Allg. Path.* II. 1879; LEBEDEFF, *Virch. Arch.* vol. 86; FÖRSTER, *Missbildungen d. Menschen* Jena 1865, *Handb. d. path. Anat.* 1863; HESCHL, *Prager Vierteljahrsschrift* 1859, '61, '68, *Jahrb. f. Kinderheilk.* XV., *Arch. d. Gesell. f. Aerzte in Wien* 1878; KUNDRAT, *Die Porencephalie* Gratz 1882, *Die Arhinencephalie* Graz 1882; KLEBS, *Ueber Hydro- u. Mikroanencephalie, Oesterreich. Jahrb. f. Pädiatrik* 1876; SCHÜLE, *Zeitschr. f. Psych.* XXVI.; BINSWANGER, *Virch. Arch.* vol. 87; WILLE, *Arch. f. Psych.* X (1880); CHIARI, *Jahrb. f. Kinderheilk.* XV.; AHLFELD, *Die Missbildungen d. Men-*

schen II. (1882); KIRCHHOFF, *Arch. f. Psych.* XIII. (1882); SPERLING, *Virch. Arch.* vol. 91; RIBBERT, *ibid.* vol. 93; DE LA CROIX, *ibid.* vol. 97; HEYDENREICH, *ibid.* vol. 100; ROSS, *Diseases of the nervous system* II. London 1883; CLELAND, *Journ. of Anat. and Physiol.* XII., XVII.

On absence of the corpus callosum:—PAGET, *Med. chir. Trans.* XXIX. (1846); SANDER, *Arch. f. Psych.* I. (1868); JOLLY, *Zeits. f. ration. Med.* XXXIV. (1869); HUPPERT, *Arch. d. Heilk.* 1871; MALINVERNI, *Gaz. delle cliniche* 1874, *London Med. Record* 1874.

On rhachischisis see Art. 632.

On defects of the spinal cord:—FROISIER, *Arch. de physiol.* 1872; ADAMKIEWICZ, *Virch. Arch.* vol. 88; LEYDEN, *Klinik d. Rückenmarkskr.* I. (1874); FLECHSIG, *Ueb. Systemerkrank.* Leipzig 1878; PICK, *Prager Med. Woch.* 1880; ROSS, *Brain* V. (1882). See also Arts. 632, 637.

631. An increased quantity of liquid may collect in the medullary tube or in the ventricles of the brain at any stage of fœtal development or after birth. If the accumulation take place very early the development of the brain may be seriously interfered with (Art. 630), its cavities are distended, and the resulting condition is described as **congenital internal hydrocephalus.** The liquid most frequently collects in the lateral ventricles, the other cavities being rarely involved. The affection is usually bilateral, though it is sometimes confined to one side.

At the time of birth the dilatation is sometimes slight, sometimes already considerable, the cranium being visibly enlarged. It often increases steadily until it reaches an enormous size, the skin is stretched and thin, and the subcutaneous veins show through its semi-transparent texture. The cranial bones become widely separated, and even though they grow to an abnormal size they do not keep pace with the distention of the whole. The fontanelles become larger and the sutures wider, and at times accessory bones make their appearance in the fibrous tissues that bridge over these spaces.

When death occurs the dura mater and the underlying membranes are found stretched to the utmost, the convolutions flattened and depressed, the sulci effaced. The brain-substance forms a mere capsule round the dilated ventricles, the thickness on the convexity of the hemispheres being sometimes not more than a few millimetres.

The liquid in the ventricles is clear and colorless or pale-yellow. The ependyma is stretched but not otherwise altered. The basal ganglia are flattened out. The fourth ventricle and the cerebellum are usually unaltered, though the former is sometimes partially dilated.

The above is the usual condition of things: in some instances however the distention of the lateral ventricles is less extreme, or it is confined to one or a part of one only. Thus one ventricle may be so distended that it is bounded only by a thin film of membrane, while the other is undilated. In like manner the fourth ventricle alone may be dilated. In these cases the general dilatation of the cranium does not

take place, the enlargement of the ventricle being accompanied by atrophy of the rest of the brain.

Extreme hydrocephalus terminates fatally. The less-marked forms are compatible with continued life. But if the dilatation is at all considerable the compressed parts of the brain undergo partial atrophy, that is to say disappearance and calcification of nerve-cells and nerve-fibres.

Great dilatation of the fourth ventricle is often accompanied by wasting of the cerebellum, pons, and medulla, or by actual disappearance of some parts of them.

Slight congenital hydrocephalus, especially if it does not increase after birth, is not altogether incompatible with a subsequent normal development of the brain.

The cause of congenital hydrocephalus is far from clear. Often no morbid changes of an inflammatory kind are to be seen, and it is usually hard to demonstrate any impediment to the outflow of venous blood from the cranium. Occasionally however thickenings of the meninges or of the plexuses are discovered, and these appear to indicate antecedent inflammation. The presence of pus-corpuscles in the hydrocephalic liquid is a surer indication. Probably in many cases the cause is to be found in some abnormal closure of the communications between the ventricular cavities and the subarachnoid spaces. These have at least in some cases been found obstructed (HUGUENIN, ZIEGLER). As moreover in such cases the pia mater over the transverse fissures at the base has been denser than usual, it is possible that the circulation in the veins of Galen was impeded. In certain instances hydrocephalus seems to be a result of rickets or of syphilis. When the skull-cavity is not dilated and the brain not compressed, while the ventricle is dilated, it appears natural to assume that the cause of the latter dilatation is the arrested development (aplasia) of the brain. The condition has been described as a dropsy *ex vacuo*.

In unilateral hydrocephalus the foramen of Monro has been found closed.

An abnormal collection of liquid in the subarachnoid tissue is called **meningeal hydrocephalus.** Of the congenital varieties some are simply due to general failure of development (agenesis, Arts. 630, 633), to local aplasia, or to some disturbance of the growth of the brain: the liquid in the meshes of the subarachnoid tissue fills the space which should have been occupied by the brain. The skull is not dilated.

In another form however the accumulation of liquid is not preceded by cerebral atrophy or aplasia, and then the brain-substance becomes compressed and the skull more or less dilated.

When the brain develops abnormally and its growth is hindered, liquid may collect in the subdural space and so fill out the cranial cavity. This condition is known as **external hydrocephalus** (VIRCHOW).

In Art. 7 we mentioned that when minor deficiencies occur in the bony walls of the skull the cranial contents protrude, and forcing out the dura mater, the cranial aponeurosis, and the scalp take the form of a rounded tumor. Such a tumor is called a **cephalocele** or **hernia cerebri.** Three forms are distinguished according to their contents. The commonest is hydrencephalocele, in which the tumor contains a sacculation of a ventricle covered with brain-substance. Encephalocele and meningocele are much rarer: in the former brain-substance and pia mater only, and in the latter the pia mater and arachnoid distended with liquid, protrude into the dural sac.

The cause of hydrencephalocele is probably an antecedent hydrocephalus. In encephalocele and meningocele there is probably some local weakness of the membranes or defect in the ossification of the cranium (ACKERMANN); in some cases the condition may be due to adhesions between the meninges and the amnion (ST. HILAIRE).

The commonest seat of cephalocele is at the lower end of the frontal suture (*hernia sincipitalis*), and about the squamous part of the occipital bone (*hernia occipitalis*). More rarely it occurs about the anterior fontanelle, the squamosal suture, the base of the skull, the orbital fissure, etc. It may continue to grow after birth.

References on hydrocephalus and cephalocele:—HUGUENIN, *Ziemssen's Cyclopædia* XII.; VIRCHOW, *Virch. Arch.* vol. 27; GUNZ, *Jahrb. d. Kinderheilk.* V. (1862); KOLLER and SCHMIDT, *ibid.* VI. (1863); HÄNEL, *ibid.* (new series) I.; AMYOT, *Med. Times* 1, 1869; DICKINSON, *Lancet* 2, 1870; BUTTENWIESER, *D. Arch. f. klin. Med.* X. (1872); PAPP and NEUPAUER, *Jahrb. f. Kinderheilk.* (new series) VII.; MAENNEL, *Jahrb. f. Pädiatrik* 1876; STEFFEN, *Gerhardt's Handb. d. Kinderkr.* V.; VIRCHOW, *Krankh. Geschwülste* I.; S. TALKO, *Virch. Arch.* vol. 50; HARRIS, *Obstetr. Trans.* VI.; HENOCH, *Charité-Annalen* IV.; BIZZOLI, *Bullet. d. scien. med. d. Bologna* 1872; RAAB, *Wien. med. Woch.* 1876; J. F. WEST, *Jahrb. f. Kinderheilk.* IX. (1876); BAUER, *ibid.* XI.; MUHR, *Arch. f. Psych.* VIII.; HEWETT, *St. Geo. Hosp. Rep.* 1873; HEINEKE, *Pitha u. Billroth's Handb.* III.; DEMME, *Jahresber. d. Jenner. Kinderspitals* Bern 1876; SZYMANOWSKI, *Langenbeck's Arch.* VI.; SPRING, *Monographie de la hernie du cerveau* Brussels 1853; G. REALI, *Ueb. d. Behand. d. angeb. Schädel- u. Rückgratsbrüche* In. Diss. Zürich 1874; ACKERMANN, *Die Schädeldifformität bei d. Encephalocele congenita* Halle 1882.

632. Corresponding to internal hydrocephalus we have a congested collection of liquid in the central canal of the cord: this is termed **internal hydromyelia** or hydrorrhachis. The canal is dilated either in parts or throughout its whole length, and the substance of the cord is accordingly thinned out. Partial dilatations are fusiform, cylindrical, or sacculate. Cases occur in which comparatively large cavities lined with cylindrical epithelium are found in the region of the posterior columns, the columns themselves being ill-developed (Arts. 637 and 650).

When the dilatation of the canal is slight the development of the cord may be normal, but where the dilatation is more marked there is

always some thinning of the nerve-substance, and the posterior columns especially are apt to suffer. Extreme localized or cystic dilatation, such as in the cervical region frequently accompanies hydrencephalocele, sometimes leads to actual discontinuity of the cord.

Another variety allied to the last takes the form of a cystic tumor-like growth protruding through the walls of the vertebral canal and appearing under the skin of the back or on the lateral or anterior aspect of the spinal column. This is known as **myelomeningocele** or **spina bifida** (Art. 7).

Lumbo sacral myelomeningocele is the commonest form. The tumor appears in the mid-dorsal line immediately above the sacrum or on the lumbar spine. It is covered with smooth or shining and sometimes thinned integument, and is of the size of a walnut or a little larger. The inner surface of the cyst is sometimes smooth, sometimes rough with outgrowths from the walls: on the upper and ventral aspect the cord is seen. It is elongated and, it may be, somewhat swollen, or attached by a broad base to the inner surface, or it is lost immediately after it enters, breaking up into a number of strands which run in the wall of the cyst.

In rare cases the cyst at birth is open, or there may be no cyst properly speaking but merely a hole in the skin surrounded by a raised border and leading by a funnel-like passage directly into the central canal of the cord.

The wall of the cyst or sack is formed chiefly of the sacculated dura mater, and the vertebral arches and spinous process are always absent at its neck. ~~Hence the name—sacral spina bifida—sometimes~~ given to the malformation.

Dorsal and cervical myelomeningoceles are much more rare, and usually smaller. The dura bulges slightly through the gap in the series of vertebral arches, while a conical or cylindrical process from the posterior aspect of the cord enters and becomes adherent to the wall of the sack. The process contains both gray and white matter, and sometimes encloses also a saccular dilatation of the central canal.

Lastly there is a form of cystic protrusion occurring in the sacral region and involving chiefly or only the membranes of the cord: it is hence described as **spinal meningocele.** A local accumulation of fluid takes place at the lower part of the subarachnoid space: the dura and the adherent arachnoid are then forced through some normal opening (such as that between two arches, an intervertebral foramen, or the lumbo-sacral hiatus) or through an abnormal one due to absence of an arch or part of a vertebral body, and thus form a protuberance on the posterior, lateral, or anterior aspect of the spine. If the liquid continues to accumulate the cyst may attain a large size. The *filum terminale* and some of the spinal nerves connect it with the cord.

It seems at first natural to suppose that the three varieties of malformation just described are due simply to morbid accumulation of

liquid in the central canal, in other words to hydromyelia combined with a local meningeal dropsy: this view has been taken by many authors (FÖRSTER, AHLFELD, and others). The anatomical characters presented by a myelomeningocele are however inconsistent with the supposition, and make it more probable that during the evolution of the central nervous system the medullary tube was imperfectly differentiated off from the surface or epidermic epiblast (RANKE, VIRCHOW, TOURNEUX, MARTIN, MARCHAND, etc.). This at least explains the fact that the cord so frequently passes out with the sack, and that the central canal sometimes opens freely into its cavity. When the cleft in the integument becomes closed over and the membranes of the cord are developed, liquid collects partly in the subarachnoid space and partly in the lower end of the central canal. It is however a question whether in some cases hydromyelia alone may not lead to myelomeningocele.

Nothing certain is known as to the causation of meningocele. Perhaps here too the malformation depends on the imperfect differentiation of the cord-substance from the epidermis.

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633. Particular parts of the central nervous system are frequently ill-developed, and in consequence remain after birth abnormally small. The cerebrum is naturally the part which has attracted most attention in this respect. When it fails to reach the minimum size met with in healthy persons the condition is spoken of as **micrencephalia**: when the cranium as a whole is likewise abnormally small we have **microcephalia.**

The average weight of the adult male cerebrum is 1375 grammes, that of the female 1245. The minimum weight for the male is 960 grammes, for the female 880; the maximum for the male 1800, and for the female 1600 grammes. The brain of a new-born infant is about 385 grammes, that of a two-year-old child 1173 grammes. The brain-weight of an infant is therefore very large relatively to its body-weight, the pro-

portion being about 14 : 100, while that of an adult is only 2.37 : 100 (VIERORDT).

Micrencephalia is usually apparent even at birth, but it becomes more obvious as the child develops: while the back part of the cranium remains stationary (microcephalia) the face grows apace and the disproportion becomes very marked. This aplasia of the brain is sometimes greater in one part than another, the anterior, lateral, or posterior region being in different cases the most stunted. As a rule however all parts are abnormally small. The gyri and sulci are generally ill-developed and abnormal in their arrangement. The subordinate or secondary sulci are usually the most defective, though cases occur in which some of the principal convolutions and fissures are entirely absent. The statistics of VOGT and JENSEN show that the weight of the brain in microcephalic patients may fall to one-third or one-fourth of the normal. The cerebellum and cerebral axis like the hemispheres are liable to be dwarfed, though they are usually less so than the latter.

C. VOGT thought than in micrencephalia we had an instance of atavism or reversion to an earlier developmental type in the *Primates*. The later researches of AEBY, JENSEN, KLEBS, FLESCH, VIRCHOW, BINSWANGER, and others have however shown that this view is untenable. Micrencephalia is an arrest or rather failure of development, an *agenesis*, due either to intrinsic causes or to injurious influences exerted on the embryo. It is accordingly very commonly found in association with other morbid alterations in the brain and other organs, and is partly a consequence and partly a concomitant of these.

Thus the micrencephalic patient may also exhibit porencephalia or ventricular hydrocephalus. Fibrous thickenings of the pia mater in some cases indicate antecedent inflammatory disorder. Often too there is some malformation of the extremities due to some injurious intra-uterine pressure; and premature synostosis of the cranial sutures, synchondrosis of the basal bones, and coalescence or cohesion of the hemispheres are also not uncommon. Of these changes some, *e. g.* porencephalia, meningeal inflammation, and premature synostosis, must occasionally be regarded not as mere concomitants of the defective cerebral development but as the primary changes which have led to it.

Less grave results of defective development are—abnormal smallness of particular lobes or gyri, and non-typical arrangement of the gyri associated with diminution (or occasionally increase) of their number. Thus in what has been called **microgyria** the surface of the hemispheres is thrown into a multitude of puckered creases or folds like those of a shirt-frill, the brain as a whole being usually malformed. Very frequently too in brains otherwise normal in size the arrangement of the convolutions is so irregular that the typical furrows and fissures that serve as our landmarks can scarcely be recognized. In rare cases the separa-

tion of the hemispheres is incomplete (TURNER, *Journ. of Anat. and Physiol.* XII. 1878).

Asymmetry of the hemispheres, affecting either the anterior or the posterior regions, is not infrequently observed. Smallness of the corpus callosum, the fornix, the thalami, the corpora striata, corpora albicantia, olivary bodies, corpora quadrigemina, etc. have also been described. The cerebellum may be no larger than a walnut, and in such cases the peduncles also are defective.

Abnormal smallness or shortness of the cord is known as **micromyelia**: the various tracts of the cord may likewise be imperfectly developed.

The causes of such local *ageneses* are sometimes undiscoverable; in other cases they are obviously connected with morbid conditions in other parts. A certain amount of hydromyelia, for example, leads to defective development of the posterior columns. Absence of the central convolutions of the cortex results in the absence or degeneration of the pyramidal tracts. Congenital absence of the cerebellum is accompanied by absence of the superior peduncle and of the red nucleus (FLECHSIG).

The loss of any of the peripheral end-organs (Art. 649) results in partial or total atrophy of the corresponding centres in the central nervous system (GUDDEN).

The posterior columns have frequently been found ill-developed (KAHLER, PICK, JÄDERHOLM, SCHULTZE), and the like is true of some of the fibres in other tracts (KAHLER, PICK, WESTPHAL, FLECHSIG, FÜRSTNER). These forms of aplasia have a special interest, as they are probably the basis of a predisposition to disease of the cord.

Heterotopia is a peculiar variety of malformation, in which masses of gray matter are found in abnormal situations. Such masses, in the form of gray nodules, are now and then met with in the ependyma of the ventricles (VIRCHOW, TÜNGEL, E. WAGNER, MESCHEDE), and in the subjacent white layer: they measure 1 to 10 mm. across and are sometimes very numerous. They have also been found in the middle of the centrum ovale (VIRCHOW, MESCHEDE), and somewhat resemble in structure the gray matter of the convolutions. Nodules of gray matter are also described (SIMON) as rising from the surface of the convolutions themselves in the form of little tumors. Heterotopia of gray matter also occurs in the cerebellum (PFLEGER), and lastly these misplaced masses have been found in the white tracts of the cerebral axis and of the cord (PICK, BRAMWELL, OSLER).

Most of those hitherto described contained ganglion-cells, but a few rather resembled the substantia gelatinosa of the cord. In the cord they are doubtless nothing more than isolated fragments of the gray matter, which frequently in the same case itself shows signs of abnormal configuration or arrangement.

Hypertrophy of the brain is rare, though it has been observed in

children and young persons: it may affect the whole or any part of the organ. It is due to excessive developmental growth, probably in the last resort arising from some abnormality in the primary rudiment of the brain. True acquired hypertrophy, not depending on congenital causes, has never been observed.

The brain and the cranium are more or less enlarged according to the extent of the hypertrophy. If the overgrowth takes place after the sutures of the skull have closed the bones in some places may be attenuated or absorbed under the continuous pressure. After death the gyri are usually found to be flattened, the ventricles narrow and appressed, and the brain-substance firm and condensed. We at present know little of the histological characters of the tissue: VIRCHOW states that the principal change is an increase of the neuroglia.

The cord in like manner is sometimes of abnormal size. Partial duplication has been met with in persons who were otherwise normally developed (LENHOSSECK, FÜRSTNER, ZACHER) or suffered from some malformation of the brain.

On microcephalia and malformation of the convolutions:—VIRCHOW, *Gesamm. Abhandl.* 1856; C. VOGT, *Arch. f. Anthropol.* II. (1867); AEBY, *ibid.* VI., VII. (1874), *Ueb. d. Verhältniss d. Mikrocephalie z. Atavismus* Stuttgart 1878, *Virch. Arch.* vol. 77; ROHON, *Arbeit. a. d. zool. Inst. zu Wien* II.; WILLE, *Arch. f. Psych.* X.; FLESCH, *Verhandl. d. phys.-med. Gesell. zu Würzburg* VIII. (1874), *Festschr. z. Jubil. d. Universität Würzburg* 1882; VIRCHOW, *Berl. klin. Woch.* 1877, *Verhandl. d. Berlin. anthrop. Gesell.* 1878; JENSEN, *Arch. f. Psych.* X.; HADLICH, *ibid.*; SANDER, *ibid.* I. (1870); KLEBS, *Sitzungsber. d. phys.-med. Gesell. zu Würzburg* 1873; SCHUTTLEWORTH, *Journ. of mental science* Oct. 1878; BINSWANGER, *Virch. Arch.* vol. 87; RETZIUS, *Hofmann und Schwalbe's Jahresber.* 1878; CHIARI, *Jahrb. f. Kinderheilk.* XIV.

On aplasia of the cerebellum and cord:—MEYNERT, *Med. Jahrb. d. Gesell. f. Aerzte* Vienna 1864; PIERRET, *Arch. de physiol.* IV. (1871-72); FISCHER, *Arch. f. Psych.* V.; HUPPERT, *ibid.* VII.; KAHLER and PICK, *Prag. Zeitschr. f. Heilk.* II. (1881), *Berl. klin. Woch.* 1879; JÄDERHOLM, *Nord. med. Arkiv* I.; A. PICK, *Prag. med. Woch.* 1880; FLECHSIG, *Ueb. Systemerkrankungen* Leipzig 1878.

On heterotopia of gray matter, hypertrophy of the brain, and duplication of the cord:—VIRCHOW, *Krankh. Geschwülste* III., *Virch. Arch.* vol. 33; MESCHEDE, *Allg. Zeitschr. f. Psych.* XXI., *Virch. Arch.* vol. 56; E. WAGNER, *Arch. d. Heilk.* 1861; TÜNGEL, *Virch. Arch.* vol. 16; PICK, *Prag. med. Woch.* 1881, *Arch. f. Psych.* VIII.; MERKEL, *Virch. Arch.* vol. 38; SIMON, *ibid.* vol. 58; SCODA, *Allg. Wien. med. Zeitung* 1859; GELMO, *Jahrb. f. Kinderheilk.* IV. (1860); STEINER and NEURECTTER, *Prag. Vierteljahrsschr.* XX. (1863); PFLEGER, *Cent. f. med. Wiss.* 1880; BRAMWELL, *Diseases of the spinal cord* Edinburgh 1884; LENHOSSECK, *Woch. d. Zeitschr. Wien. Aerzte* 1858; FÜRSTNER and ZACHER, *Arch. f. Psych.* XII.; OSLER, *Journ. of Anat. and Physiol.* XV. 1881 (so-called medullary neuroma).

VIRCHOW (*Gesamm. Abhandl.* 1856) found in a child 3 years old a brain weighing 1911 grammes, in another of 13 the brain weighed 1732. LANDOUZY (*Gaz. méd. de Paris* 1874) describes a brain of 1590 grammes in a boy of 10, and ZIEGLER has recorded one of 1857 grammes in a young woman of 20.

634. All the malformations of the brain above described, when they

are not incompatible with life and growth, give rise to more or less grave disorder of its functions. Where the malformation is great mental development fails, and a condition of **idiocy** is the result. There is however no one variety of malformation which can be assigned as the anatomical basis of idiocy; there is in other words no special 'idiotic brain.' General arrest of development, dropsical dilatation of the ventricles, local defects or imperfections, all may result in idiocy. In other instances idiocy may accompany very slight and apparently unimportant abnormalities, such as heterotopia of gray matter, absence or smallness of the corpora albicantia, corpus callosum, fornix, thalamus, optic nerves, corpus striatum, pineal body, or olivary body, irregularity of the gyri, asymmetry of the hemispheres, etc.: or the brain may be so far as we can see perfectly normal, or hypertrophic through increase of the neuroglia. Lastly, ischæmic and inflammatory destructive processes affecting the cortex sometimes induce idiocy. On the other hand grave malformations such as we have just mentioned, and even others apparently more serious, have existed without giving during life any functional evidence of their presence.

In cretinism as in sporadic idiocy no special and characteristic defect of the brain can be demonstrated.

Cretinism is as we have seen (Art. 623 *a*) a disorder of development occasioned by some unknown miasmatic influence, and manifested in the imperfect growth of the skeleton and the disproportionate size of the soft parts. Idiocy more or less pronounced is a frequent though not invariable symptom, but malformation of the brain is not more general or constant than in idiocy without cretinism.

BENEDIKT some time ago asserted that in **criminals** certain peculiarities of the configuration of the cerebral surface were constantly met with, and inferred that criminals were practically to be regarded as an anthropological variety of the race. Their brains resemble in some points those of lower animals, and were characterized by a tendency of the sulci to run one into the other, so that they were continuous at points where in normal brains they would be bridged over or interrupted by convolutions. This hypothesis is however untenable. Apart from the difficulty of settling the definition of the term criminal, investigation has shown that BENEDIKT's anomaly of the sulci occurs in persons who have never committed crime or come under the criminal law (BARDELEBEN).

The like holds for the anomalies and malformations of the brain found in certain **insane** and **epileptic patients.** They are none of them peculiar or pathognomonic of nervous or mental disease, inasmuch as they also occur in persons whose mental functions are perfectly normal. All we can say is—that anomalies of brain-structure, both grave and trifling, are more frequent in persons who exhibit mental peculiarities or defects than in those whose minds are normal. Thus heterotopia

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CHAPTER XCIII.

DISORDERS OF CIRCULATION.

... quantity of blood contained in the vessels of the cerebro- ... is subject to very considerable physiological variations. It ... hen the system is functionally active than when it is at rest: ... ns of the basilar arteries give rise to a pulsatile movement of ... ity of the brain, and its surface likewise rises during expira- ... sinks during inspiration. Local hyperæmia of a particular ... uses an efflux to other parts of the lymph from the circumvas- ... annels and of cerebrospinal liquid from the subarachnoid ... and from the ventricles. When hyperæmia is general space is ... for the excess of blood by the efflux of cerebrospinal liquid into ... mphatics of the head, neck, and trunk, and into the venous ... s of the dura mater.

Morbid **congestion** or arterial hyperæmia of the brain and cord is ... asioned when the activity of the heart is greatly and abnormally in- ... ased, or when the resistance to dilatation of the afferent arteries or of ... e arterioles of the meninges and nerve-substance is morbidly dimin- ... hed. In the latter case the hyperæmia may remain local.

Passive hyperæmia or **engorgement** takes place when the return of venous blood from the cranial cavity and the spinal canal is checked, as it is for instance in certain diseases of the heart and lungs. Local engorgement may be due to intracranial thrombosis, or to tumors, exudations, etc. passing upon the veins.

Venous engorgement of the brain or cord is most apparent in the meninges, whose vessels are more or less distended with blood, and owing to the transparency of the membranes can be followed to their minutest ramifications. The meninges have but few capillaries, and hence the injection of the venules is most marked, though a few of the arterioles are also distended. It must however be kept in mind that the appearances after death are far from representing exactly the conditions that prevailed during life: as soon as death takes place the blood is in a measure free to pass out of the cranium and the vertebral canal, while that which remains tends to sink to the parts that are most dependent.

Hyperæmia of the white matter is recognizable *post mortem* only by the distention of the small veins: on section they allow their contents to

exude as variously-sized drops of blood. A general reddening of the tissue from dilatation of the capillaries is very uncommon, owing to the fact that the coagulation or post-mortem rigidity of the white matter squeezes most of their contents out of the capillaries, while the non-transparent nature of the coagulated white matter prevents the red tint from shining through.

In the gray matter the minuter venules and capillaries may remain filled with blood, the latter giving rise to a diffuse or mottled reddening of the tissue.

Anæmia of the central nervous system is manifested by the emptiness of the arterioles and venules of the pia mater, and the pallor of the gray matter. The white matter on section shows few or no drops of blood on its surface. This anæmia of brain and cord may be part of a general anæmia, or may be due to a morbid congestion of other organs or parts of the body (collateral anæmia). Or again it may result from spasmodic contraction, thickening, or other obstruction in the afferent arteries, or to changes within the cranium and vertebral canal which interfere with the entrance of blood, *e. g.* changes which diminish the space within these bony cavities, such as subarachnoid effusion, dropsy of the ventricles, tumors, hæmorrhages beneath the dura mater, and so on.

Anæmia of the brain and cord is general or local according to the inducing condition. Local anæmia may for instance be caused by closure of a branch of the sylvian artery (middle cerebral), or by the pressure on the cord of a dislocated vertebra or a tumor of the dura mater.

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636. The brain and spinal cord are especially liable to **hæmorrhage**, both by diapedesis and by rupture (Art. 27). In simple congestive hyperæmia some amount of capillary bleeding is not uncommon, and such bleeding is an almost invariable accompaniment of acute inflammatory disorder of the brain. In both cases the extravasations appear as round or oval specks of the size of a pea or smaller, often mottling the cut surface in a remarkable way. The extravasated blood lies partly in the brain-tissue, partly in the sheaths of the vessels. In the latter

position the small collections of blood are often described as miliary dissecting aneurysms.

In pyæmic encephalitis bacteria are sometimes to be seen in the vessels, and look as if they gave rise to capillary hæmorrhage partly by obstructing and partly by destroying the walls of the vessels. In other cases the capillaries have undergone fatty degeneration.

When the arteries are obliterated by sclerotic thickening of the intima, by thrombosis, or by embolism, the hæmorrhages are not usually very extensive; these changes more frequently give rise to a number of small isolated patches of extravasation.

Extreme venous engorgement, due for example to obstruction of the jugular veins or thrombosis of a sinus in the dura mater, frequently gives rise to capillary and venous hæmorrhages situated chiefly in the pia mater and the ependyma of the ventricles. In the former situation they are are sometimes so massive that the subarachnoid and subpial spaces are largely filled with blood. Engorgement within the brain, such as results from large tumors or old extravasations, usually leads to the formation of numerous small circumscribed patches, lying around the capillaries and small veins either in the sheaths of the vessels or in the nerve-substance itself.

Wounds, compressions, contusions, and concussions of the brain and cord due to traumatic violence give rise to bleeding whose extent is of course dependent on the number and magnitude of the ruptured vessels.

Extensive spontaneous hæmorrhage (**apoplexy**) results from the rupture of an artery, and that only takes place when the arterial wall has from degenerative or inflammatory change lost its normal power of resistance (Arts. 297–300). Aneurysmal dilatation (Art. 303) usually though by no means always precedes rupture. Increased pressure within the arteries (so-called 'high tension'), such as generally accompanies the hypertrophied heart and contracted kidney of chronic nephritis or arteriosclerosis, is apt to lead to the rupture of diseased vessels, but not of healthy ones.

Spontaneous arterial hæmorrhage takes place most frequently in and about the region of the basal ganglia and the internal capsule. It is less common about the pons, crura, cerebellum, and centrum ovale. It is least common on the convexity of the hemispheres.

This inequality of distribution depends on the fact that the arteries of the base are subject to a higher blood-pressure than the smaller vessels which pass from the arterial network of the pia mater into the gray matter of the cortex. This is especially true of the branches of the sylvian artery which supply the basal ganglia and the internal capsule.

Arterial hæmorrhage results in disintegration of the nerve-tissue and ganglia over a more or less extensive area, and in compression of the parts surrounding the area. Only in the smallest capillary hæmorrhages can the nerve-tissue escape, and then it is simply compressed by accumu-

lation of blood in the circumvascular sheaths. Rupture of the smallest arteries produces hæmorrhagic foci varying from the size of a pea to that of a hazel-nut; in the case of the larger branches rupture may destroy entire segments of brain-tissue, such as the greater part of the basal ganglia of one side, together with part of the contiguous white substance, or the whole white centre of one occipital lobe.

A recent hæmorrhagic patch forms a soft dark-red coagulated or pulpy mass, containing fragments of disintegrated nerve-tissue. When the hæmorrhage is large the remainder of the brain is anæmic, the convolutions more or less flattened by pressure, and the furrows effaced. Round the chief focus lie a varying number of smaller foci mottling the cut surface, and due to the disturbance of the circulation set up by the primary hæmorrhage. If the rupture takes place in the neighborhood of a ventricle, blood may pass into its cavity and thence through the transverse fissures into the subarachnoid space.

Blood extravasated into the cortex is apt to collect beneath the pia mater and may also penetrate to the subarachnoid space. In hæmorrhage from meningeal arteries these spaces are naturally the main seat of extravasation, the brain-substance being affected only in a secondary manner. When the arachnoid membrane is ruptured we have also subdural accumulations of blood.

As coagulation takes place, the hæmorrhagic mass contracts and the watery portions of the blood are in part removed by means of the blood-vessels and lymphatics. The initial compression of surrounding parts is thus gradually diminished and at length ceases. At the same time the clot changes color and becomes reddish-brown. Presently some of the coloring-matter (hæmoglobin) is absorbed, tinging with yellow the parts around. At length the whole mass disintegrates (Art. 68), the detritus is in course of time absorbed (Arts. 638, 642), and the space so vacated is filled up either by exuded liquid or by the contraction and falling together of its walls. In the latter case a corresponding dilatation of the subarachnoid space or of the ventricles must take place. When the space is filled with liquid we have what is called an **apoplectic cyst**, when the space is effaced by contraction of its walls we have an **apoplectic cicatrix**. In either case there is usually some thickening and induration of the walls (Art. 639), which are stained of a yellow, brownish-red, or brown color, while some of the pigment derived from the extravasated blood remains unabsorbed as brown flakes and granules of ferric hydrate, with perhaps a few particles or crystals of hæmatoidin. The induration is due partly to fibrous hyperplasia of the sheaths of the blood-vessels, partly to proliferation of the neuroglia.

When the hæmorrhage is small and confined to the sheaths of the vessels, and so does not involve any destruction of nerve-tissue, the products of disintegration of the extravasated blood are for the most part

carried off by the circumvascular lymphatics, though granules of pigment frequently lie for a long time embedded in the adventitial sheaths.

Our knowledge of the genesis and history of spontaneous hæmorrhage in the brain is largely due to CHARCOT (*Les maladies des vieillards* Paris 1867, *Diseases of old age* (New Syd. Soc.) London 1881). He affirms that small or **miliary aneurysms** (described by VIRCHOW in *Virch. Arch.* vol. 3; see also BOUCHARD, *Pathology of cerebral hæmorrhage* London 1872) are always present, and sometimes in great numbers, in cases of arterial hæmorrhage. They are due he thinks to periarteritis, which leads to infiltration and thickening of the adventitial and pial sheaths, and to atrophy of the muscular coat. The author finds that CHARCOT'S statement applies only to a certain number of cerebral and spinal hæmorrhages. The aneurysmal dilatation does not always precede rupture: and as to the cause of the dilatation he agrees with ZENKER (*Naturforscherversammlung in Leipzig* 1872), EICHLER (*D. Arch. f. klin. Med.* XXII.), COATS (*Trans. internat. med. congress* I. London 1881), LÖWENFELD (*Arbeiten aus dem pathologischen Institut zu München* 1886), and others, that it may be due to atheromatous degeneration, or even to primary degeneration of the muscularis alone. This last is not always of an amyloid nature, as ROTH maintained (*Corresp. f. Schweizer Aerzte* 1874); at least cases occur in which the muscular fibres are either simply absent or exhibit a fatty or hyaline change which gives no iodine-reaction (PAGET, *Surg. Path.* London 1863). The accumulation of cells and the fibrous thickenings in the sheaths of the vessels described by CHARCOT are doubtless in some instances of a secondary nature. See CHARLEWOOD TURNER, *Trans. Path. Soc.* XXXV. 1884.

The '**miliary dissecting aneurysms**' (first described by KÖLLIKER in 1849) are most frequently met with in cases of acute inflammatory congestion. The term is strictly-speaking incorrect, inasmuch as the blood does not collect between the media and the adventitia (Art. 309), but between the vessel-wall and the pial sheath.

Both ruptured and unruptured aneurysms of the cerebral vessels may be filled up with white or laminated clot and so become obliterated.

637. **Œdema** of the brain and cord is characterized chiefly by abnormal moistness of the gray and white matter, so that it has a glistening appearance on section. Owing to the peculiar structure of the central nervous system the dropsical liquid accumulates not so much in the parenchyma of the nerve-tissue itself as in the wide lymph-spaces which it contains. These are chiefly the pial sheaths of the vessels, the ventricles, the central canal of the cord, and the subarachnoid and pial spaces. We thus distinguish œdema of the nerve-tissue from œdema of the pial sheaths of the vessels, of the membranes (*hydrops meningeus*), of the ventricles (*hydrops ventriculorum* or *hydrocephalus internus*), and of the central canal (*hydromyelia*). In dropsy of the sheaths of the vessels the circumvascular lymph-spaces are distended with liquid, so that the vessels appear insulated as they run through the tissue. Sometimes small cysts are thus formed (SCHLESINGER) with a vessel running axially through them.

In œdema of the membranes there is always an increase of the subarachnoid liquid, more rarely of that in the subdural space (*hydrocephalus*

externus). Over the surface of the brain the sulci appear somewhat widened out. This change sometimes extends over the whole brain and cord, sometimes is limited to a particular region: in the latter case the boundary of the dropsical part is indefinite or it is so sharply defined that the distended subarachnoid and pial spaces resemble cysts (cystic or vesicular œdema). These dilatations are met with both on the surface and in connection with the processes of the pia mater which lie inside the ventricles, namely the telæ choroideæ and their plexuses. The latter especially sometimes carry cysts of the size of a bean or larger and filled with clear liquid. The cyst-walls consist of vascular connective tissue covered externally with flat polygonal epithelium and internally with endothelium. The cavity of the cyst is often traversed by vessels and delicate fibrous bands. Small cysts of this kind are of no great importance, but the larger ones may cause serious compression of the brain and lead to disturbance of its functions.

Ventricular dropsy implies the distention and dilatation of one or all the ventricular cavities: hydromyelia leads to cylindrical, fusiform, globular, or more rarely saccular dilatations of the central canal.

The causation of accumulations of liquid within the central nervous structure is not entirely the same as that of dropsy in other organs: to a certain extent they are of a peculiar nature, and to understand them we must somewhat widen our notion of what dropsy implies.

An **œdema of engorgement** may take place over say the whole of the brain whenever the outflow of venous blood from the cranial cavity is impeded. This occurs suddenly when the heart is paralyzed, as in some cases of typhoid (Buhl, Kräpelin), when the veins of the dura mater are occluded by thrombosis, etc. Chronic disease of the heart or lungs impeding the circulation will in like manner give rise to chronic œdema. Acute engorgement usually leads to accumulation of liquid in the parenchyma of the brain as well as in the subarachnoid tissue, chronic engorgement usually in the latter only or chiefly.

Local œdema of engorgement is very common round about hæmorrhagic foci, tumors, localized venous thromboses, etc. When by reason of a tumor or of inflammatory change the outflow of blood from the choroid plexuses is impeded, and the outflow of cerebrospinal liquid from the ventricles and central canal is at the same time checked, liquid will accumulate to a greater or less extent in these cavities and distend them. According to Langhans fusiform and even saccular dilatations of the central canal are sometimes produced by this cause; they project into the posterior longitudinal fissure of the cord and usually take a downward direction. He also states that clefts or spaces containing effused liquid occasionally appear in the gray matter of the posterior commissure and of the anterior and posterior horns; these may fitly be described as **dropsical lacunæ.**

The so-called **hydræmic dropsy** occurs chiefly in connection with nephritis, and affects the brain-substance as well as the membranes.

Inflammatory œdema is set up within the substance of the brain and cord in the neighborhood of foci of inflammation, sometimes also around tumors and patches of softening. In the membranes it may be the chief symptom of a slight meningitis, though it accompanies almost every form of localized disease of the superficial parts of the central nervous system. In the ventricles and central canal it results from inflammatory changes in the vessels of the plexuses and the ependyma, and is sometimes very extensive. It is acute or chronic according to the affection which induces it. When the inflammatory effusion in the ventricles is abundant the convolutions are compressed against the skull and flattened, while the blood and lymph are gradually squeezed out of the enveloping membranes.

Acute general **congestive œdema** of the brain is said to be commonest in children and as a result of acute congestive hyperæmia. The sudden congestion increases the intra-cranial pressure, and so compresses the capillaries and veins that the outflow of blood from the meninges is hindered: in this way secondary engorgement and œdema are produced (HUGUENIN).

It is not possible to distinguish sharply between congestive and inflammatory œdema: on the contrary it is highly probable (JÜRGENSEN) that so-called congestive œdema often represents merely an early stage of a rapidly fatal inflammation (Arts. 652, 653).

When the brain and cord diminish in size, the space they leave unoccupied is usually filled up by the collection of liquid in the subarachnoid space: this is described as **meningeal dropsy** *ex vacuo*. Sometimes the ventricles are at the same time dilated. The volume of the brain may diminish rapidly as in extreme anæmia, profuse diarrhœa, infantile marasmus, etc. or slowly and gradually as in senile atrophy. The like happens to a limited extent when parts of the brain or cord lying just beneath the ependyma or pia mater are lost in consequence of some destructive process. When the nerve-substance in the interior of the central organs undergoes atrophy the space vacated is sometimes filled by liquid gathering in the circumvascular channels of the affected region itself. This is especially apt to occur when the atrophy has been preceded by abnormal dilatation of the vessels or distention of the lymphatics within the brain, so that the circumvascular lymph-spaces are already abnormally capacious. If the condition is wide-spread, affecting a considerable number of vessels, the brain on section appears riddled with perforations and the condition is referred to as *état criblé* (Art. 643).

Extensive loss of substance in the interior of the brain or cord, whether due to hæmorrhage, softening, or inflammation, leads (after absorption of the detritus) to the formation of cavities which are generally

filled up in part by clear or turbid liquid: these are described as **cysts.** If they are small and numerous the apparent perforation of the tissue is also described as *état criblé* ('Gruyère cheese condition': see SAVAGE and WHITE, *Trans. Path. Soc.* XXXIV. 1883).

Vesicular œdema or cysts of the pia mater would appear to depend on the presence of closed lymph-spaces, congenital or acquired, in the pia mater and subarachnoid tissue.

An interesting affection of the cord called **syringomyelia** should be mentioned in this connection. The term is applied to a condition in which fissures and cavities occur, chiefly in the posterior gray commissure and about the median plane, and often extending longitudinally over a considerable distance. Not infrequently the excavation extends into the posterior horns, traversing them sometimes transversely sometimes obliquely, or into the posterior columns; very rarely extending as far as the anterior horns, the anterior commissure, or the lateral columns.

These fissures and cavities may occur in any part of the cord, they have even been observed in the medulla oblongata (SCHULTZE). They are always enclosed by a delicate more or less cellular neurogliar tissue, and are in part due to the breaking down of some gliomatous proliferation of this tissue. Their contents are either clear liquid or a kind of hyaline jelly. The proliferation which precedes their excavation starts as a rule in the neuroglia about the central canal, though it may also originate in remoter portions of either gray or white matter. From the facts at present before us it seems likely that the starting-point in most cases is some congenital histological anomaly in the posterior commissure, which interferes with the closure of the central canal and so with the development of the posterior columns. In many cases syringomyelia is thus a consequence of congenital hydromyelia (LEYDEN), and that either because some abstricted remnants of the medullary tube persist behind the central canal, or because malformation of the central canal is associated with histological changes in the parts about it which predispose to abnormal proliferation and subsequent disintegration of tissue (Art. 650). With reference to the supposed abstriction and persistence of parts of the medullary tube it should be mentioned that several observers (SCHÜPPEL, PICK) have recorded instances of duplication and even triplication of the central canal for some part of its length, each tube being lined with cylindrical epithelium.

Various explanations of syringomeylia have been given. SIMON and F. SCHULTZE refer it to the disintegration of proliferous neuroglia. LANGHANS maintains that obstructions to the flow of blood or lymph, such as are caused for example by the growth of tumors, give rise to dilatations and even sacculations of the central canal. Such saccular diverticula extend through the posterior columns and adjacent parts usually in a downward direction, and so form as it were a segment of a second canal behind the central canal. Dropsical lacunæ may also be formed by the collection of gelatinous liquid in the gray commissure

and the posterior horns. The appearances would thus be accounted for. LEYDEN regards syringomyelia as resulting from congenital hydromyelia in the manner described in the text. WESTPHAL takes a like view, which is rendered at least possible by the fact that the central canal even in a fœtus of the fifth month still extends to the posterior margin of the cord.

ZIEGLER agrees with those who think the affection is essentially due to an excavation of proliferous neuroglia. LANGHANS is no doubt right in stating that tumors of the cord and medulla give rise to very remarkable dilatations of the central canal, and it is not hard to believe that actual diverticula are occasionally produced. But these should properly be considered as cases of hydromyelia, and they do not exclude the possibility of an excavation of proliferous tissue; to this latter it would perhaps be well to limit the term syringomyelia. Probably too we shall be right in referring the whole process to a congenital anomaly of development, the proliferation depending on some morbid structure of the neuroglia, accompanying or following upon defective closure of the canal or defective elaboration of the gray or white matter in its neighborhood.

References on syringomyelia and duplication of the central canal:—NONAT, *Archives générales* 1838; GULL, *Guy's Hosp. Reports* VIII. (1862); HALLOPEAU, *Archives générales* 1871–72; VIRCHOW, *Virch. Arch.*, vol. 27; KESTEVEN, *St. Barth. Hosp. Reports* VIII. (1872); WESTPHAL, *Arch. f. Psychiatrie* V. (1874), *Brain* VI. (1883); SIMON, *ibid.*; LEYDEN, *Klinik d. Rückenmarkskr.* II. 1877, *Virch. Arch.* vol. 68; STRÜMPELL, *Arch. f. Psych.* X.; FRIEDREICH, *Virch. Arch.* vols. 26, 27; GRIMM, *ibid.* vol. 48; LANGHANS, *ibid.* vol. 85; REISINGER, *ibid.* vol. 98; F. SCHULTZE, *ibid.* vol. 87; SCHÜPPEL, *Arch. d. Heilk.* VI. (1864); PICK, *Arch. f. Psych.* VIII.; WITKOWSKI, *Arch. f. Psych.*, XIV. (1883); FÜRSTNER and ZACHER, *ibid.* XIV.; TAYLOR, *Trans. Path. Soc.* XXIX. (1878), XXXV. (1884); WHIPHAM, *ibid.* XXXII. (1881); KRAUSS, *Virch. Arch.* vol. 101; HARRIS, *Brain* VIII. (1886).

On cysts of the meninges, choroid plexus, etc.:—ZENKER, *Virch. Arch.* vol. 12; HAECKEL, *ibid.* vol. 16; LUSCHKA, *Die Adergeflechte d. mensch. Gehirnes* Berlin 1855; ROKITANSKY, *Path. Anat.* III. London 1850; RIPPING, *Cystoide Degen. d. Hirnrinde*, *Allg. Zeitschr. f. Psych.* vols. 30, 32 (1874–65); SCHOPFHAGEN, *Wiener Sitzungsber.* LXXIV. (1876); SCHLESINGER, *Arch. f. Psych.* X.; ARNDT, *Virch. Arch.* vols. 63, 72.

According to BUHL (*Henle u. Pfeuffer's Zeitschr. f. rat. Med.* IV. (1858)) the amount of water in the brain in typhoid fever increases up to the beginning of the third week, the increase amounting to 9 or 10 per cent above the normal.

CHAPTER XCIV.

SIMPLE AND DEGENERATIVE ATROPHY.

638. In all **degenerative processes** affecting the central nervous system the nerve-elements are the first to disintegrate and disappear, while the neuroglia frequently persists unchanged or actually increases.

Ganglion-cells atrophy by simple shrinking of their protoplasm without visible change of structure; when they lose their processes they appear as little shrunken specks (Figs. 257, 258, Art. 640) and at length disappear altogether: this is **simple atrophy**.

Pigmented ganglion-cells as they shrink appear to be still more

FIG. 250. DEGENERATION OF CELLS AND FIBRES FROM THE CEREBRAL CORTEX.

(*From the border of an encephalitic patch eight days old : the preparation macerated in Müller's fluid and then teased out* : × 300.)

a, swollen and hyaline ganglion-cells, with processes already splitting up

a_1, pale denucleated cell beginning to split into fragments

a_2, cell resolved into oil-globules

b, axis-cylinder swollen up and splitting

c, normal ganglion cell

deeply tinted; indeed it sometimes looks as if the actual amount of pigment were increased during the atrophic process. This form has been called **pigmentary atrophy**.

In acute destruction of the ganglion-cells, such as occurs in the neighborhood of inflamed areas, after sudden compression, anæmic and hæmorrhagic softening, and so on, the cells and their processes frequently swell up (Fig. 250) and become pale and hyaline (a). Some-

times vacuoles appear, and the nuclei partake of the general swelling. After a time the cells split up and dissolve away (a_1), the nuclei at the same time disappearing. **Fatty degeneration** of the cells may also occur (a_2) under the same conditions, but it is more common in cases where chronic or recurrent disorder of the circulation leads to defective nutrition of the cells. In such cases it may be the only change that is perceptible: it may occur in patches or extend over the cortex. Fatty change of this kind is met with in many forms of mental disease.

When the ganglion-cells have once perished, whether from inflammation, anæmia, sudden compression, or other cause, and do not at once dissolve, they sometimes undergo **calcification** (Fig. 251), becoming as it were tightly crammed with particles and spherules of calcareous matter. FRIEDLÄNDER found a calcified ganglion-cell thirteen days after a

FIG. 251. CALCIFIED GANGLION-CELLS AND FIBRES.

(From the brain of a hemiplegic idiot with unilateral hydrocephalus: × 300.)

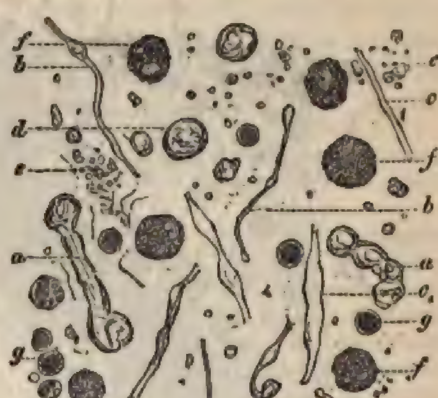

FIG. 252. DEGENERATION OF THE CORD FROM PRESSURE.

(White matter teased out: × 300.)

a, nerve-fibre with coagulated myeline
b, axis-cylinder with myeline attached
c, naked axis-cylinder, c_1 another much swollen
d, free globules of myeline
e, free detritus
f, granule-spheres (cells crammed with detritus)
g, small round-cells (leucocytes)

wound of the part. In chronic diseases the cells sometimes take on a glistening wax-like appearance, a change which has been described as sclerosis of the ganglion cells.

In the **degeneration of nerve fibres** (at least of the medullated kind) the medullary sheath is the first part to disintegrate. When for example a portion of the brain or cord is destroyed by traumatic violence or by anæmic or inflammatory softening, the disintegrated tissue contains nerve-fibres whose sheath consists of myeline in a peculiar state of coagulation (Fig. 252 *a*), together with naked or sheathless axis-

... myeline (d), and small spheres ... disintegration of myeline. The ... sometimes greatly swollen (c_1), ... that they have been described as ... and are absorbed; sometimes ... myeline accumulate at certain points ... varicose appearance (b) from an-

... in cases that are chronic or less ... that are severed from their

638. In all d... system the ner... while the neu... degeneration it is sooner or later

Ganglion-c... without visible ... appear as little ... disappear alt...

Pigmented ...

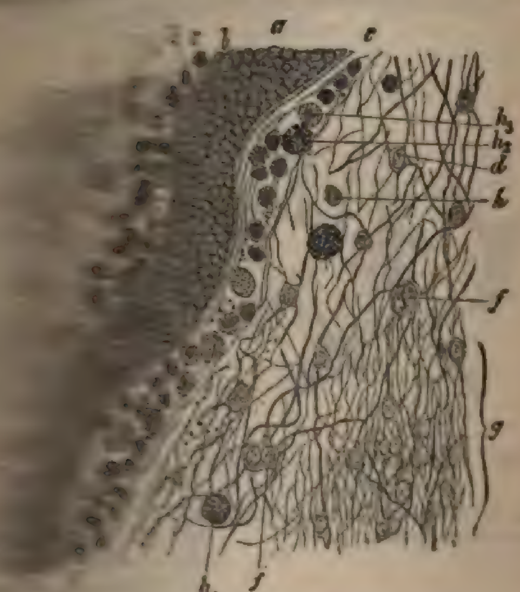

FIG. ... A CASE OF MULTIPLE SCLEROSIS OF THE BRAIN.
(*From the* ... *osmic acid and teasing* : × 200.)

a, swollen and ...
a_1, pale ... fragm...

g, sclerotic tissue
h, lymphoid cells and leucocytes
h_1, cells containing a few oil-globules
h_2, fat-granule cells
h_3, pigment-granule cells

deeply ... ment wa... called pig...

In ac... neighbo... hæmorr... quently ... of liquid and of white blood-cells from the ... detritus dissolves in the exudation and is ... remainder is taken up chiefly by the white ... myeline-carriers and fat-granule cells ... The latter are always present when disin- ... If blood should have escaped from the

vessels during the process, pigment-granule cells (Fig. 253 h_1) will also be found.

The free detritus and the carrier-cells are in the course of time conveyed into the circumvascular lymph-channels (Fig. 253 *c*) of the affected region and by them removed.

When the degeneration is extensive not only the neighboring lymphatics but also those more remote are crammed with granules and granule-carrying cells. If these reach the meshes of the pia mater or the subarachnoid space they give the tissue a milky and turbid appearance.

Corpora amylacea (Art. 61), which are normally met with in the brain-tissue, are found in increased numbers where degeneration has taken place.

Regeneration of the nerve elements of the brain and cord appears never to occur, at least in man. When ganglion-cells and the nerve-tracts corresponding to them are once destroyed, the functions they performed can only be restored by the substitution of equivalent centres and tracts capable of functionally replacing them.

The above-mentioned form of disintegration of the myeline of nerve-fibres is usually described as fatty degeneration, inasmuch as the myeline-detritus after a time gives the microchemical reactions of fat.

When the tissues of the brain and cord, with their membranes and lymphatics, are found to contain granule-carrying cells, it may in general be regarded as evidence that disintegration of nerve substance has taken place at some place or other. According to JASTROWITZ (*Arch. f. Psych.* II.) this applies only to persons more than seven months old. From the fifth month of gestation to the seventh month after birth such granule-cells occur normally in various parts of the central nervous system, depending on the stage of growth: they appear to be connected with the development of the medullary nerve-sheaths. According to BOLL the material for the formation of these sheaths is brought to the fibres by migratory cells. Formerly their presence was supposed to indicate a morbid change described as **congenital encephalitis.** VIRCHOW has however re-asserted (*Berl. klin. Woch.* 46, 1883) the pathological nature of the granule-cells found in the brain of new-born infants, arguing that the granules give the microchemical reactions of fat but not those of myeline, that they are not constantly found, and that they are accompanied by swelling of the neuroglia-cells and multiplication of nuclei, and that occasionally some degeneration of nerve-tissue is present. The granule-cells are either scattered diffusely or grouped in clusters which form opaque white patches on the grayish-red surface of the fœtal brain, and are quite visible by the unaided eye.

Not infrequently the pia mater about the base of the brain exhibits a deep-brown **staining.** It is usually due to an exceptional development of the stellate pigment-cells normally found in the pia mater, and is therefore not pathological. Morbid pigmentation of the membrane is as we have seen sometimes caused by hemorrhagic effusions.

The mode in which the **amyloid concretions** are produced is not certainly known. CECI has recently (*Transunti d. real. accad. dei Lincei* V.) called attention to the fact that they do not always give the iodine-reaction, while they are stained brown or black by perosmic acid, differing in this from ordinary amyloid

substance. In their double refracting power and in their reactions they resemble myeline, and CECI suggests that they may consist of or be derived from that substance.

The question of the regeneration of the tissues of the central nervous system and especially of the cord has frequently been the subject of experimental enquiry. H. MÜLLER experimented on lizards and fishes (*Ueb. Regeneration d. Wirbelsäule u. d. Rückenmarkes* Frankfort 1864), MASIUS and VANLAIR *Mém. de l'acad. de Belgique* XXI. (1870)) on frogs, while BROWN-SÉQUARD (*Gaz. méd.* 1849, '50, '51), EICHHORST and NAUNYN (*Arch. f. exp. Path.* II.), DENTAN (*Rech. sur la régénération de la moëlle épinière* In. Diss. Berne 1875), and SCHIEFFERDECKER (*Virch. Arch.* vol. 67) used dogs. Some of the results were negative, others pointed to functional and histological regeneration of the severed cord. Nevertheless it cannot be considered as proved that this regeneration takes place in mammals.

References on the behavior of ganglion-cells and nerve-fibres in degeneration:—VIRCHOW, *Virch. Arch.* vols. 10, 44, 50; LEYDEN, *Klinik d. Rückenmarkskr.* 1874–76, *Zeitschr. f. klin. Med.* I. (1879); OBERSTEINER, *Wiener med. Jahrb.* III., IV. (1879); JAHN, *Arch. f. Psych.* VIII.; ZENKER, *Arch. f. Ophthalm.* II.; MÜLLER *Beitr. zur path. Anat. d. Rückenmarkes* Leipzig 1871; CHARCOT, *Maladies du syst. nerv.* Paris 1877–80; *Diseases of the nervous system* (New Syd. Soc.) London 1876–80; MESCHEDE, *Virch. Arch.* vol. 34; MÖBIUS, *Schmidt's Jahrb.* 190, 193 (a summary of recent memoirs on nervous diseases); WIEGER, *Virch. Arch.* vol. 78 references on hyaline degeneration of cerebral vessels); HADLICH, *ibid.* vol. 46; SALVIOLI, *Rivista clin. di Bologna* 10, 1878; ROTH, *Virch. Arch.* vol. 53; FRIEDLÄNDER, *ibid.* vol. 88. The last three authors refer specially to calcification of ganglion-cells either as an accompaniment of degeneration or as an independent affection. VIRCHOW met with it chiefly as a consequence of concussion of the brain. On senile degenerative changes in the cells of the cortex see KOSTJURIN and HESS, *Wiener med. Jahrb.* 1886.

639. When a large area of nerve-tissue is destroyed the **neuroglia** is apt at the same time to undergo partial necrosis, or at least to show evidence of fatty degeneration in its tissue-cells (Fig. 253 *e*). In like manner the endothelium of the pia mater and of the blood-vessels may become fatty. When the destruction of tissue is less extensive the nerve-elements alone persist, while the neuroglia with its vessels and their supporting fibrous structures remain intact.

After absorption of the products of disintegration of the nerve-elements the neuroglia of the white matter of the brain has the appearance of a network of anastomosing stellate cells (Fig. 254 bb_1). The fibrils of these cells are very fine, and in hardened sections at least have a granular appearance, which is most marked in recent preparations where the degeneration is not advanced. When the absorption of the nerve-tissue is incomplete, the meshes of the connective tissue contain particles of detritus and granule-carrying cells (Fig. 254 *c*).

The white matter of the cord in degeneration resembles that of the brain (Fig. 255 *B*), but the network (*c*) of connective tissue which originally surrounded the parallel nerve-fibres appears much more regular and at the same time stouter. The meshes contain either liquid or the

detritus of the nerve-fibres together with granule-cells (d) and a few leucocytes.

The neuroglia of the gray matter, like that of the white, may persist after the nerve-elements have disappeared. The tissue in hardened sections appears granular (Fig. 258) and beset with the nuclei of neuroglia-cells. In the cortex of the brain fibrils make their appearance which at their intersections exhibit small masses of protoplasm with or without nuclei. Here and there cells can be seen giving off procesees resembling the fibrils. As degeneration proceeds a delicate granular meshwork (Fig. 260 *a* Art. 642, Fig. 271 Art. 650), with cells placed at some of the intersections, is all that remains. Ultimately this too disappears, so that nothing persists but the blood-vessels (Fig. 260 *b*, Fig. 254 cc_1).

In many cases the persisting neuroglia itself ultimately perishes. In

FIG. 254. SECTION THROUGH THE MARGIN OF A PATCH OF SOFTENING IN THE BRAIN.

(*Hardened in Müller's fluid, stained with hæmatoxylin and carmine, and mounted in Canada balsam*: × 250.)

A normal tissue
- a, nerve-fibres cut across at various angles
- b, normal neuroglia-cells
- b_1, persisting neuroglia-cells
- c, blood-vessel
- c_1, blood-vessel with thickened sheath

B degenerate tissue
- d, extravasated but unaltered white blood-cells
- e, fat-granule cells which have lost their fat during the treatment of the section with alcohol and clove oil

others it remains quiescent or undergoes hyperplasia. So far as can be made out the process begins by subdivision and multiplication of the persisting nuclei of the tissue-cells (Fig. 253 *f*, Fig. 254 *B*). This is followed by cell-multiplication and fibrillation, and the resulting new tissue appears like a felted mass of delicate translucent fibrils and nucleated cells, enclosing particles of detritus and liquid (Fig. 253 *g*,

Fig. 256 *b*). Some of the fibrils are connected with the neuroglia-cells, forming processes as it were; others seem to have no such connection (Fig. 253).

Frequently the walls of the blood-vessels, and especially the adventitial tissue, take part in the hyperplastic process. The vessels then look as if beset and studded with proliferous cells, and the adventitia is thicker and more densely fibrous than usual (Fig. 254 c_1).

So long as a degenerating patch contains detritus of nerve-tissue it appears white and opaque and is of soft consistence. If the disintegration is extreme it may be almost diffluent on section. After absorption of the products of disintegration the tissue becomes gray and translucent. When hyperplasia of the neuroglia ensues a gray gelatinous patch is formed; such patches are occasionally described as instances of **gray degeneration.**

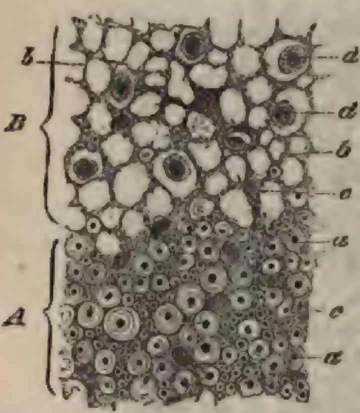

FIG. 255. ASCENDING DEGENERATION OF THE CORD (RECENT).

(*Section taken from a cord which had been severely compressed ten weeks before: hardened in Müller's fluid, stained with hæmatoxylin and carmine, and mounted in Canada balsam:* × 250.)

A normal white matter
B degenerate white matter

a, normal nerve-fibres
b, neuroglia
c, neuroglia-cells
d, fat-granule cells (fat dissolved out)

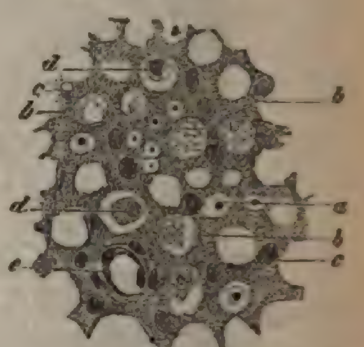

FIG. 256. ASCENDING DEGENERATION OF THE CORD (ADVANCED).

(*Section taken from a cord severely compressed eighteen months before: prepared as in Fig. 252:* × 250.)

a, section across nerve-fibres
b, hyperplastic neuroglia
c, nuclei of neuroglia-cells
d, fat-granule cells (fat dissolved out)

When the new-formed fibrils are scanty and their meshes wide and filled with liquid, the patch is soft; on section it allows the liquid to escape and retracts below the general surface. If the fibrils are abundant and the resulting felted mass close-meshed, the patch is firm and dense. These two varieties correspond to soft or **gelatinous degeneration** and firm gray degeneration or **sclerosis.** The sclerotic tissue by con-

traction may become tough and cicatricial, but this requires months and probably years.

The behavior of the blood-vessels varies according to the form of the degenerative process. As a rule however in the later stages hyperplasia of the adventitia and thickening of the vessel-walls take place.

The more intimate **structure of the neuroglia** or supporting framework of the nervous system, and the significance of its several elements, are matters which are still under discussion.

SCHWALBE distinguishes three constituents, namely (1) the epithelium of the ventricles and central canal, (2) the neuroglia, which in life forms a homogeneous cementing substance between the nerve-elements, but after death is resolved by coagulation into delicate reticular fibrils, (3) a 'granular substance' which forms a very close-meshed network and is composed of neuro-keratin (EWALD and KÜHNE). All of these, he says, are derived from epithelial structures. The neuroglia it is true contains flattened (endotheloid) cells, but they are to be regarded as migratory cells which have become modified.

KÖLLIKER, DEITERS, JASTROWITZ, BOLL, LÖWE, GOLGI, FRIEDMANN, and others assign the neuroglia to the connective tissues, and give as its constituents a fibrillar network, a granular matrix or ground-substance, and cells both stellate and simple.

SCHWALBE'S account of the neuroglia does not agree with the experience of pathologists. It is a tissue which to some extent is *sui generis*, some of its properties resembling those of no other structure; but it must nevertheless be classed with the connective tissues.

Both gray and white matter contain besides nerve-cells round or oval cells with scanty protoplasm and numerous fine processes either radiating in all directions (stellate cells) or running more or less parallel (Fig. 253 *ef*, Fig. 254 c_1, Fig. 268). These were first described by DEITERS and are called **Deiters' cells.** The number of the processes and the form of the cells vary much in different parts.

There are also certain rounded or polygonal cells without processes, which are either undeveloped Deiters' cells or migratory cells.

The ground-substance surrounding the cells consists of a finely-granular reticulate structure through which the processes of the cells ramify. It is not yet certain whether all the fibrils that are seen communicate with cells. In the white matter the granular structure is scanty or absent, in the gray matter it is abundant, and the nerve-fibres and ganglion-cells seem as if embedded in it. It is questionable however whether the ground-substance is granular during life. According to GIERKE (*Neurol. Centralb.* 1883, *Arch. f. mikrosk. Anat.* XXVI. 1885) it is homogeneous and transparent.

SCHULTZE and RUMPF (*Cent. f. med. Wiss.* 1878) have found that in hyperplasia of the neuroglia, where a dense felted mass of fibrils is produced, the so-called neuro-keratin of KÜHNE does not increase in quantity, and the new fibrils react to digestive agents just like fibrous tissue.

The terms gray degeneration and sclerosis have been used as if they were equivalent terms. Strictly speaking σκληρος means hard and dry, and the term **sclerosis** should be limited to hardening accompanied by loss of moisture (Art. 650).

References on the histology of the central nervous system:—HENLE and MERKEL, *Zeitschr. f. rat. Med.* (3d series) vol. 34; LOCKHART CLARKE, *Phil. Trans.* 1851, '58, '59, '62; DEITERS, *Unters. über Gehirn u. Rückenmark* Brunswick 1865;

MEYNERT, *Bau d. Grosshirnrinde* Neuwied 1869; GERLACH, *Stricker's Man. of Histology* II. (New Syd. Soc.) London 1872; JASTROWITZ, *Arch. f. Psych.* II., III.; BOLL, *ibid.* VII. (1873); LÖWE, *ibid.* VII. (1877); STIEDA, *Zeitschr. f. wiss. Zool.* XVIII., XIX., XX., XXIII., XXV.; RANVIER, *Comptes rendus* LXXVII. (1873), *Histologie du syst. nerv.* Paris 1878, *Arch. de physiol.* XV. 1883 (structure of neuroglia); GOLGI, *Rivista clinica* Nov. 1871, *Arch. ital. de biologie* III., IV.; SCHWALBE, *Handb. d. Augenheilk.* (*Gräfe and Sämisch*) I., *Lehrb. d. Neurol.* Erlangen 1881; FRIEDMANN, *Jahrbücher f. Psych.* 1883; EWALD and KÜHNE, *Verh. d. nat. med. Vereines zu Heidelberg* I.; Duke KARL THEODOR of Bavaria, *Virch. Arch.* vol. 69; J. WEISS, *Med. Jahrbücher* 1878; TURNER, *Journ. of Anat. and Physiol.* XIII. 1879 (descriptive summary of recent memoirs); SCHOPFHAGEN, *Jahrbuch f. Psych.* III. (1881); KLEIN and NOBLE SMITH, *Atlas of Histology* London 1880, *Quain's Anatomy* II. London 1882; HOLLIS, *Journ. of Anat. and Physiol.* XVII., XVIII., XIX.

640. **Simple atrophy.** This term is applied to those changes in the brain and cord which are characterized by dwindling and partial disappearance of the nerve-elements without any marked textural alteration either preceding or following. The atrophy is either general or at least extensive, or it is confined to particular parts of the brain and cord.

Atrophy of the **cerebrum** is the commonest example of the extensive form; the whole or the greater part of the hemispheres diminishing more or less in volume, the gyri becoming narrower, and the sulci with the subarachnoid spaces wider and filled with liquid. Not infrequently the ventricles also are dilated.

Atrophy of the **cerebellum** or of the **medulla** and **cord** is much less common: cases are however recorded in which the cerebellum was so shrunken that its volume was less than half the normal and its gyri were almost filiform. In most instances the atrophy is not uniformly diffused, but is most evident in one or two of the lobes or in particular convolutions. The atrophied parts are usually firmer and denser than the healthy parts.

Atrophy of the pons, of the medulla, and of the cord, is sometimes symmetrical, sometimes unsymmetrical, and may affect the nerve-tracts as well as the ganglion-cells.

The forms of local atrophy most amenable to microscopical investigation are those which are met with in the anterior horns of the cord and in the motor nuclei of the medulla (bulbar nuclei), and which form the anatomical basis of certain nervous diseases variously named by clinical observers.

The anterior horns (Fig. 257) of the cord consist of a tissue whose characteristic elements are large multipolar ganglion-cells (a) and numerous tracts of medullated nerve-fibres (b), whence the anterior roots (b_1) of the spinal nerves take their origin. Between these elements is a complex texture of stout and slender nerve-fibres (d), the whole being embedded in a delicate nucleated neuroglia (e).

In simple **atrophy of the anterior horns** (Fig. 258) the ganglion-cells and then the nerve-fibres are lost; so far as can be made out they

simply dwindle and disappear. The ganglion-cells (*a*) lose their processes and shrink up into small pigmented lumps: when these perish nothing remains but a few grains of pigment, and even this may be ultimately removed by absorption. At length all but a very few of the

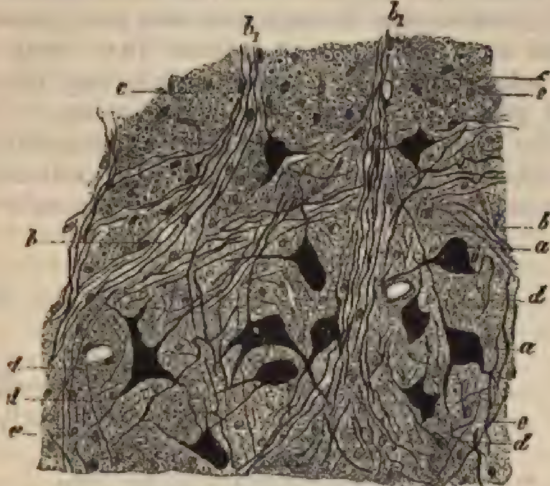

FIG. 257. LEFT ANTERIOR HORN (NORMAL) AT THE LEVEL OF THE FOURTH CERVICAL NERVE.

(*Hardened in Müller's fluid and alcohol, stained with hæmatoxylin and carmine, and mounted in Canada balsam:* × 150.)

a, multipolar ganglion-cells
b, horizontal nerve-tracts within the gray matter
b_1, anterior roots
c, cross-sections of nerves in the adjacent white matter
d, nerve-fibres cut across more or less obliquely
e, nuclei of neuroglia-cells

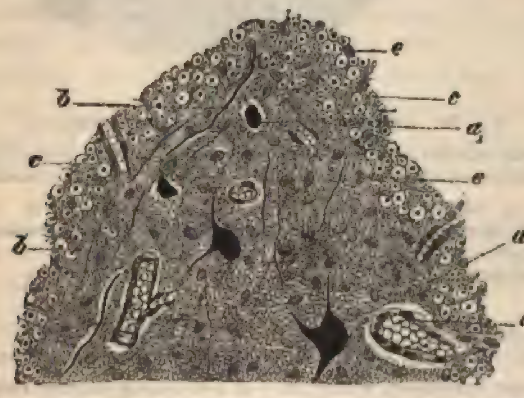

FIG. 258. LEFT ANTERIOR HORN (ATROPHIED) AT THE LEVEL OF THE FOURTH CERVICAL NERVE.

(*From a woman aged 40 who died of ascending atrophy of the anterior horns: prepared as above:* × 150.)

a, normal ganglion-cells
a_1, atrophied ganglion-cells
b, intact nerve-fibres in gray matter
c, cross-sections of nerves in adjacent white matter
d, blood-vessel

cells and fibres ($a\,a_1\,b$) disappear, and the anterior horn comes to consist chiefly of neuroglia.

Simple uncomplicated atrophy is not accompanied by any change of the connective tissue, and there is no trace of inflammatory mischief: moreover it is only when the nerve-fibres are involved and their medullary sheath is undergoing disintegration that even granule-cells are detected, and these in very small number (Art. 638). Sometimes **secondary sclerosis** follows. Simple atrophy may therefore be described as a primary affection involving simple loss of the nervous elements of the gray matter of the anterior horn; it leads to atrophy of the anterior roots of the spinal nerves, and paralysis with atrophy of the muscles supplied by them. It may attack any portion of the anterior

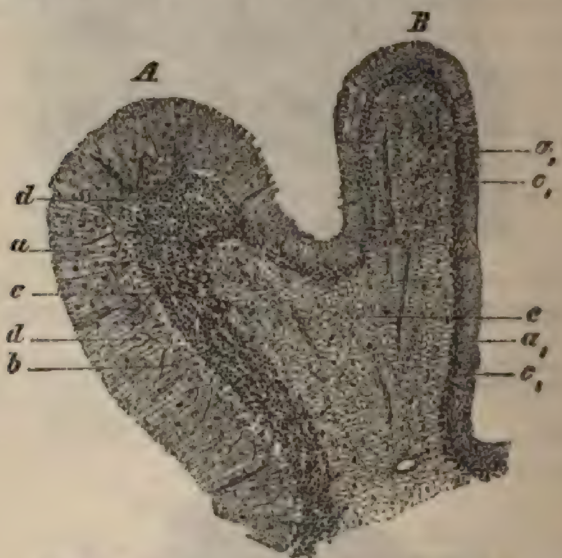

FIG. 259. ATROPHY OF THE CORTEX OF THE CEREBELLUM.

(From a man aged 25 who died in an epileptic fit: section hardened in Müller's fluid and alcohol, stained with hæmatoxylin and carmine, and mounted in Canada balsam; × 25.)

A, normal, *B*, atrophied gyrus

a, normal external layer
a_1, atrophied external layer
b, normal intermediate layer
c, normal, c_1 atrophied granular layer
d, Purkinje's cells
e, medullary (white) centre

columns, but most frequently begins at the upper or the lower extremity and thence extends. In the former case the motor nuclei in the medulla are usually soon involved, while in the ascending forms this is naturally a late symptom. The sensory nuclei in the medulla and the posterior columns of the cord are in general unaffected.

This peculiar affection may thus be characterized as a simple disappearance of the ganglion-cells of the motor centres of the cord and medulla. When it extends over the greater part of the length of the

cord it gives rise to a portion of the group of diseases spoken of as chronic atrophic spinal paralysis (*poliomyelitis anterior chronica*) and progressive muscular atrophy; when it involves the nuclei of the medulla it leads to some of the affections known collectively as chronic progressive bulbar paralysis and Duchenne's paralysis. Descending atrophy of the anterior horns is in general associated with degeneration in the pyramidal tract (Art. 647). When the atrophy begins in the lumbar cord this degeneration does not take place.

A similar disappearance of nerve-cells and nerve-fibres takes place both in the **basal ganglia** and in the **cerebral cortex.** When extensive it leads to a very marked loss of bulk in the parts affected. This loss of bulk is due partly to the entire disappearance, partly to marked dwindling, of the nerve-elements. In the cortex it is sometimes uniformly and widely diffused, sometimes in isolated patches.

The **white matter** like the gray is also liable to atrophy, which is either primary or secondary to atrophy of gray matter. When the bulk of a portion of the brain or cord is markedly diminished, the atrophic process extends to the white matter, and microscopic examination shows that some of the nerve-fibres in the latter have entirely disappeared while others have plainly undergone diminution of their thickness. In the disseminated or patchy form of atrophy the medullary white centre of the cerebrum often contains minute areas within which the tissue has a perforated or cribriform appearance; the nerve-fibres having disappeared a loose meshwork of neuroglia is all that remains. The adventitial lymph-spaces are in general dilated (Art. 637).

Atrophy of the laminæ of the **cerebellum,** when it is at all marked, is chiefly due to thinning of the cortical layers, though the medullary centre also suffers in a less degree. As the cells and nerve-fibres disappear the external (or molecular) layer (Fig. 259 a) of the cortex is reduced to a third or fourth (a_1) of its original thickness. The cells of Purkinje (d) and their processes disappear entirely, and with them the slender intermediate layer (b). Lastly the granular layer (c), losing its nerve-cells and fibres, becomes reduced to a mere film (c_1).

Loss of volume alone is not a certain mark of atrophy of the brain. Thus in infants suffering from chronic diarrhœa the brain may shrink so rapidly that the cranial bones overlap one another, but this is due in great measure simply to abstraction of liquid from the brain and its membranes.

Atrophy of the anterior horns of the cord can be certainly demonstrated only by examining a series of sections. The ganglion-cells are by no means uniformly distributed in different segments of the cord, and thus it may happen that a single section of a perfectly normal cord shows very few ganglion-cells, while neighboring sections show them in abundance.

Many authorities speak of pigmentary atrophy of the ganglion-cells as distinct from simple atrophy; but it does not appear that there is ever any real or marked increase of pigment in the cases they describe. As ganglion-cells normally containing pigment become smaller the pigment does not disappear, and they ac-

cordingly seem to have more of it in proportion to their size. Non-pigmented cells scarcely ever exhibit any pigment as they atrophy. It must however be admitted that occasionally after the disappearance of the cells the amount of pigment seems to increase.

Atrophy of the large ganglion-cells of the anterior horns is followed by atrophy (**amyotrophy**) of the corresponding muscles; but all muscular atrophy is not dependent on loss of the ganglion-cells. ERB, SCHULTZE, and others have described cases in which after recent atrophy of the anterior horns of gray matter the anterior nerve-roots were still intact, though the muscles showed signs of degeneration. From this it would appear that the muscles perish more rapidly than the nerve-fibres. Many authors affirm that loss of the anterior ganglion-cells is accompanied by an increase of the neuroglia. This is occasionally the case, but by no means uniformly: very marked atrophy may be unattended by any such increase. It is worth mentioning that after the total disappearance of the nerve-elements from a section of the anterior horns small granular masses remain, interspersed among the cells and fibres of the neuroglia. This would go to show that the granular-looking substance of the gray matter does not belong wholly to the nerve-fibres and ganglion-cell-processes, a view recently re-affirmed by RANVIER (*Arch. de physiol.* I. 1883).

Atrophy of the anterior horns with or without sclerotic change is often regarded as a chronic inflammation and described as *poliomyelitis anterior chronica.* In like manner ischæmic softening is sometimes regarded as a poliomyelitis. The genesis and course of these affections make it obvious that they are non-inflammatory and that such terms are inappropriate.

References on simple atrophy of the anterior horns and bulbar nuclei:— CHARCOT and JOFFROY, *Arch. de physiol.* 1869; PIERRET, *ibid.* II. (1875); CHARCOT and GOMBAULT, *ibid.*; DUCHENNE and JOFFROY, *ibid.* IV. (1870); CHARCOT, *ibid.* *Diseases of the nervous system* London 1876–80; KESTEVEN, *St. Barth. Hosp. Rep.* XIII. (1878); SCHULTZE, *Virch. Arch.* vol. 75; CORNIL and LÉPINE, *Paralysie gén. spinale ant. subaiguë, Gaz. méd. de Paris* 1875; JARISCH, *Viertelj. f. Derm. u. Syph.* VIII. (1881); ERB and SCHULTZE, *Arch. f. Psych.* IX.; VIERORDT, *ibid.* XIV.; GOLTDAMMER, *Berl. klin. Woch.* 1876; DÉJÉRINE, *Arch. de physiol.* VI. (1883); see also Art. 647, references on amyotrophic lateral sclerosis.

References on the structure of the cerebellar cortex and cerebellar atrophy:— DENISSENKO, *Arch. f. mikros. Anat.* XIV.; OBERSTEINER, *Allg. Zeitschr. f. Psych.* vol. 27, *Biolog. Centralb.* III. (1883); GOLGI, *Arch. ital. p. l. mal. nerv.* 1874, *Rivista sperim. di freniatria* 1882, 1883; FIEDLER, *Zeitschr. f. rat. Med.* II. (1861); DUGUET, *Gaz. hebdom.* 1862; MEYNERT, *Med. Jahrb. d. Gesell. d. Aerzte in Wien* 1864; PIERRET, *Arch. de physiol.* IV. (1871–72); E. CLAPTON, *Trans. Path. Soc.* XXII. (1871); OTTO, *Arch. f. Psych.* IV.; FISCHER, *ibid.* V.; HUPPERT, *ibid.* VII.; BISCHOFF, *ibid.* XII.

641. Some of the conditions included under the general term atrophy are directly dependent on **aplasia** or agenesis (Arts. 630 and 633) of parts of the brain and cord. Many atrophies detected only in years of maturity are in fact aplasias dating from the fœtal period. Other atrophies affect nervous structures which have from the beginning been ill-developed or ill-organized. The greater number of cases of cerebellar atrophy (Art. 640) unassociated with inflammation or tumor certainly belong to this latter class, as do also those cases of shrinking of the cerebrum in which close examination of the convolutions and their structure

shows that the atrophy coexists with local aplasias, such as partial defects of the gyri, etc. Atrophies of the cord, also, are frequently found associated with anomalies of its development.

When simple atrophy occurs without any visible cause in patients who have a family history of nervous disease, it is natural to suppose that the nerve elements have had some intrinsic weakness of constitution which led to their premature decay and disappearance: and the same supposition is permissible even in cases where there is no such history.

GUDDEN and his pupils have shown that sensory as well as motor centres undergo atrophy and lose their ganglion-cells if at birth and or in infancy the peripheral end-organs or nerves are destroyed. The explanation is perhaps this—that in the absence of the end-organ the corresponding central organ is not called on to perform its function and so wastes, or at least fails to attain to complete development.

Loss of peripheral end-organs in later life is only to a slight extent followed by similar atrophy. Thus after amputation of the limbs no marked changes take place in the cord, the number of ganglion-cells and nerve-fibres is apparently unaltered. In a few cases the corresponding half of the cord has appeared to become smaller, probably from thinning of the nerve-fibres. At the same time it must be kept in mind that in fifty out of every hundred persons the cord is more or less unsymmetrical (from incomplete decussation of the pyramids), and this makes it difficult to be sure that in a given case asymmetry is due to pathological causes.

Loss of the eye and optic nerve leads after a time in the human subject to atrophy of the corresponding parts of the optic tract. When blindness has lasted for a number of years the atrophy is said (HUGUENIN) to extend up to the occipital lobe.

Senile atrophy of the brain, which is not at all uncommon, seems to be due in the first place to mere outwearing and decay of the nerve-elements, and in part also to diminution of the natural nutritive processes (see KOSTJURIN and HESS, *Wiener med. Jahrb.* 1886). Cerebral atrophy in younger patients reduced and weakened by disease is doubtless due chiefly to disordered nutrition.

Localized atrophy of nerve-cells and fibres within particular circumscribed regions is at times demonstrably induced by atheromatous and hyaline thickening of the vessel-walls (Art. 642), or by occlusion and obliteration of the circumvascular lymph-channels from extravasation of blood or hyaline deposit. As regards the various forms of nervous atrophy met with in persons who have long suffered from disordered circulation, we must assume that the general cause has led to the particular effect. Disease of the heart or of the lungs, chronic inflammation of the meninges (Arts. 655, 656), and intracranial tumors, all act in this way; in the latter case local compression leading to local anæmia (Art. 644) assists the more general causes Lastly we must recognize

as causes of atrophy the many injurious agencies which reach the central nervous system by way of the blood, and so damage its constituent elements. As examples we may mention lead (VULPIAN, DÉJÉRINE, MONAKOW, POPOW, and others), and alcohol when taken constantly and for a long time.

GUDDEN (*Arch. f. Psych.* II., *Graefe's Arch. f. Ophthalmologie* XX., XXI., XXV., *Naturforscherversammlung in Eisenach* 1882) was the first to show that the extirpation of peripheral or central end-organs in young animals is followed by atrophy of the corresponding central or peripheral end-organs respectively and of the conducting tracts. Thus extirpation of one cerebellar hemisphere induces atrophy of the restiform body and its three nuclei on the same side and the olivary body on the opposite side. Extirpation of one anterior quadrigeminal body leads to blindness and proportionate wasting of the nerve-fibres of the optic tract on the opposite side. This method enables us to determine the central nuclei, the course, and the connections of the various cerebral and spinal nerves, and the connections between the nuclei of the cerebral axis, the cerebrum, and the cord. FOREL (*Arch. f. Psych.* VII.), MAYSER (*ibid.*), GANSER (*ibid.* XIII), FÜRSTNER (*ibid.* XII.), and MONAKOW (*ibid.* XII., XIII.) have applied the method, and thereby greatly increased our knowledge regarding the nuclei and tracts of the cerebral axis. MONAKOW (*Arch. f. Psych.* XII.) showed that extirpation of the visual centre in the occipital cortex in new-born rabbits is followed by **atrophy** of almost the entire **visual tract,** *i. e.* the corresponding part of the corona radiata (optic radiations of Gratiolet), the external geniculate body, the lateral (latticed) stratum of the external nucleus of the thalamus, to a less extent the anterior quadrigeminal body of the same side, the chiasma, and the opposite optic nerve. Extirpation of the eyeball leads to atrophy of the same parts, most marked however in the optic nerve of the same side and in the anterior quadrigeminal body of the opposite side. According to HAAB a like atrophy or rather aplasia is met with in cases of anophthalmia.

Our knowledge of the secondary degenerations of the visual tract is however still very defective, and minute investigation of the histological changes involved is much to be desired. Probably the first change is a disintegration of the medullary sheath of the nerve-fibres (Art. 646): the axis-cylinder appears to persist for a time. GUDDEN, SCHMIDT-RIMPLER, PURTSCHER, SAMUELSOHN, BAUMGARTEN, MARCHAND, and others have shown that atrophy of the optic nerve is after a time accompanied by wasting of the decussating bundles of fibres on the inferior or ventral aspect and of the non-decussating bundles on the dorsal aspect of the optic tract. We do not yet know how far this process of wasting may extend. SAMUELSOHN followed it up to the external geniculate body: HUGUENIN states that it extends to the occipital lobe. The descending atrophy induced by destruction of the visual centre in the cortex (hemianopsia) has not been fully investigated. LEBER thinks that in adults the trunk of the optic nerve does not atrophy after a cortical lesion, and only after a period of years when it is the optic tract that is destroyed. HOSCH (*Klin. Monatsbl. f. Augenheilk.* XVI.) alone seems to have actually observed atrophy of the optic nerve after destruction of the occipital lobe. It would appear from what we have said above that in the case of the optic nerve we may have an ascending atrophy, but the like has not been observed in the case of other sensory nerves. The only analogue is apparently the atrophy of the posterior columns of the cord observed to follow destruction of the posterior nerve-roots, and we might add the instance of ascending atrophy of the auditory nerve extending to the temporal lobe, which

HUGUENIN describes as having occurred in a patient who had been deaf for many years.

References on ascending atrophy of the visual tract:—LEBER, *Graefe and Saemisch's Handb.* V.; GUDDEN, *Arch. f. Ophthalm.* 1879; HAAB, *Beiträge z. Ophthalm., Festschrift für Horner* Wiesbaden 1881; KELLERMANN, *Beilage z. klin. Monatsbl.* 1879; PURTSCHER, *Graefe's Arch. f. Ophthalm.* XXVI. (1880); SAMUELSOHN, *Berl. klin. Woch.* 1880; BAUMGARTEN, *Cent. f. med. Wiss.* 1878; MARCHAND, *Graefe's Arch.* XXVIII.; MAUTHNER, *Gehirn und Auge* Wiesbaden 1881; DRESCHFELD, *Brain* IV. (1882).

On hemianopsia and destruction of the cortical visual centre see Art. 625.

DICKINSON (*Journ. of Anat. and Physiol.* III. 1868), DRESCHFELD (*ibid.* XIV. 1880), VULPIAN (*Arch. de physiol.* 1868), LEYDEN (*Klinik d. Rückenmarkskr.* II.), DÉJÉRINE and MAYER (*Gaz. méd. de Paris* 1878), and others have described cases of atrophy of the motor and sensory centres and tracts in the cord after **amputations** of the limbs. Objections may be taken to some of their statements, but it would appear that the posterior roots, posterior horns, and posterior columns may occasionally atrophy: the ganglion-cells and nerve-fibres do not disappear outright but become abnormally small and thin.

It is questionable whether in persons who in adult life have lost a limb the corresponding centres in the cortex ever undergo atrophy. SANDER (*Cent. f. med. Wiss.* 1875), LUYS (*Gaz. des hôp.* 1876), BOURDON (*Recherches clin. sur les centres mot. des membres* Paris 1877, *Bull. de l'acad. de méd.* XII. 1883), and others have described such cortical atrophies, but it must be remembered that the width of the convolutions varies greatly even in persons otherwise normal. CHARCOT, FERRIER, and others have failed to find unmistakable instances. DAVIDA (*Virch. Arch.* vol. 88) and EDINGER (*ibid.* vol. 89) have found that when limbs are congenitally absent there is atrophy of the spinal nerve-roots, the corresponding gray matter, and the lateral columns of the cord, and in some cases (EDINGER, GOWERS) even of the corresponding cortical centres.

VULPIAN (*Maladies du syst. nerv.* Paris 1879), DÉJÉRINE (*Gaz. méd. de Paris* 1879), MONAKOW (*Arch. f. Psych.* X. 1880), POPOW (*Virch. Arch.* vol. 93), and others state that in paralysis from **lead-poisoning** there is degeneration not only of the muscles and peripheral nerves but also of the ganglion-cells of the cord and brain. It does not appear certain that lead gives rise to any primary atrophy of the central nervous system, though apparently there is no doubt that in lead-poisoning the brain may contain a large proportion of the metal, and that the affection may be accompanied by grave and chronic mental disorders. For reference see ROSS, *Diseases of the nervous system* II. London 1883, and ROBINSON, *Brain*, VIII. 1885.

642. **Ischæmic and hæmorrhagic softening.** The vessels of the brain and cord are peculiarly liable to morbid changes. Sclerosis and atheroma are more common in them than in those of almost any other organ, while the small arteries and capillaries of the central nervous system and its membranes might almost be called the favorite seat of hyaline degeneration. Fatty and calcareous change are exceedingly common, the latter being sometimes so extensive and so great that on section the vessels stand out from the brain-substance as little rigid tubes. Moreover corpuscular matters passing from the heart into the arterial system, and atheromatous detritus or fibrinous coagula from the

ascending aorta, are very readily swept through the cervical into the cerebral arteries.

The consequence is that it is very common for the arteries of the brain or cord to be suddenly or gradually occluded, the accident being followed by grave disturbance of the circulation and nutrition of the corresponding regions.

The arteries of the brain and cord have no arterial anastomoses within the nerve-substance, and thus after the closure of one of them collateral circulation is very slowly and imperfectly established. This is especially the case when the neighboring arteries are already rigid and obstructed by atheromatous or hyaline change in their walls.

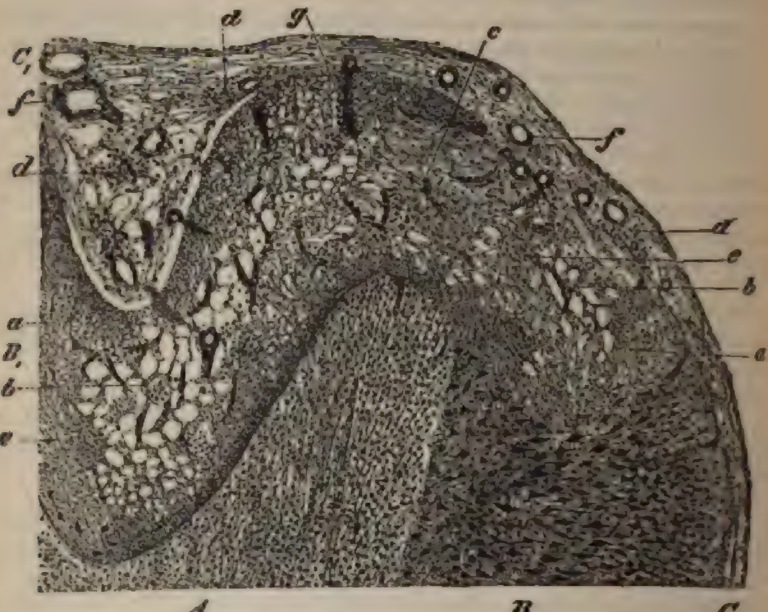

FIG. 260. ISCHÆMIC SOFTENING OF THE CORTEX OF THE BRAIN.

(*From the brain of an idiot: hardened in Müller's fluid and alcohol, stained with hæmatoxylin and carmine, and mounted in Canada balsam:* × 25.)

A, white centre *B*, normal cortex B_1, softened cortex
C, normal pia mater C_1, thickened pia mater

a, softened part of the cortex without ganglion cells, the neuroglia still remaining in places
b, part with little but the capillary network remaining
c, condensed fibrous-looking tissue
d, groups of cells in the subpial and subarachnoid spaces
e, patch containing leucocytes, fat-granule cells and pigment-cells
f, small blood-vessel
g, groups of cells in the circumvascular space

Engorgement, stasis, and hæmorrhage all lead to local anæmia or **ischæmia** of the particular regions affected. Hæmorrhage need not be at all large; even the smallest extravasations, confined it may be to the

pial sheaths of the vessels, have their effect, and other matters, such as products of disintegration, when they collect in these sheaths may by compression render the vessel impermeable to the circulation.

Lastly, compression of the nerve-substance by tumors, exudations, etc. (Art. 644) leads frequently to local anæmia or ischæmia.

When such temporary or permanent ischæmia gives rise to necrosis of the substance of the brain or cord, **softening** of the necrosed region speedily takes place. If the ischæmia is unaccompanied by hæmorrhage the tissue remains pale and at first only becomes softer and more brittle: this process is therefore described as **white softening.**

After a few days the substance of the organ is (owing to the rapid disintegration of the nerve-elements and the escaped liquid from the vessels) transformed into a pulpy mass, containing the products of disintegration described in Art. 638 together with fat-granule cells of every conceivable form.

In the course of weeks the process of liquefaction steadily advances, and at length nothing remains of the nerve-substance but a liquid mass rendered turbid by detritus and fat-granule cells. The blood-vessels usually persist (Fig. 254 *c*, Fig. 260 *b*), and thus the liquid appears as if lodged in the meshes of a delicate network of capillaries. After some months the liquid becomes clear, owing to the absorption of the products of disintegration.

Around the patch of softening the neuroglia proliferates and gives rise to **sclerotic thickening,** though this is seldom very marked. It is most apt to occur when the patch is small, the patient young, and the softening not due to arterial sclerosis. Often after weeks or months no considerable proliferation is discoverable, the softened patch being surrounded by a zone in which the nerve-elements are in process of degeneration and the tissue accordingly more or less interspersed with granule-cells.

The vessels within the softened patch become in part obliterated. Cellular and fibrous hyperplasia sometimes takes place in the pial sheaths both of the collapsed and of the permeable vessels.

When hæmorrhage accompanies the ischæmic softening the products of disintegration of the extravasated blood mingle with those of the nerve-substance and give the patch a red, yellow, rusty, or brown tint. The process is then described as **red** or **yellow softening.** The mass thus contains pigment-granule cells, and after a time flakes of yellow or brown pigment and occasionally crystals of hæmatoidoin are deposited in the surrounding tissue.

On ischæmic softening see EISENLOHR (*Arch. f. Psych.* IX. 1878, on acute affections of the medulla and pons), KLEBS (*Prag. med. Woch.* 1879).

On hyaline degeneration of cerebral vessels see WEDL (*Wiener Sitzungsber.* XLIII. 1863), ARNDT (*Virch. Arch.* vol. 49), LUBIMOFF (*ibid.* vol. 57), BENEDIKT (*ibid.* vols. 64, 72), KOLESSNIKOW (*ibid.* vol. 85), NEELSEN (Arch. d. Heilk. XVII.

1876), OTTO (*Arch. f. Psych.* XVI., on aneurysms of the vessels of the cord), and references in Art. 636.

643. The size of a patch of softening depends on that of the vascular territory which has been deprived of blood, and consequently varies much in different cases. The smallest patches may be too small for the unaided eye, the larger may involve whole convolutions, important sections of the centrum ovale or of the basal ganglia, or even entire lobes.

The smaller patches after a time take the form of little cavites filled with clear liquid, and when numerous give the tissue a cribriform or sponge-like appearance. When the softening has occurred round a small arterial branch the space left vacant on absorption of the products of disintegration is often filled up by accumulation of liquid in the adventitial lymph-channel belonging to the vessel, which latter then looks as if it ran through a wide lymph-sac resembling that caused by simple localized lymphatic stagnation or engorgement. The condition in which the nerve-tissue is thus as it were riddled with small cavities is commonly described as an *état criblé* (compare also Art. 637).

The contents of large **cysts of disintegration** due to ischæmic softening are seldom quite clear, the absorption of the solid detritus being a very slow process, while at the borders of the softened region the disintegration of nerve-substance usually goes on to some extent for months or years after the initial lesion.

When such large cysts lie just under the pia mater or at least not very deeply, the overlying tissue in general sinks in and leaves a subpial or subarachnoid space which soon fills with liquid. The depressed surface looks opaque and white or tinged with yellow or brown. On section the softened patch is found to contain a milky (or sometimes pigmented) liquid traversed by shreds of tissue which are for the most part collapsed or still permeable vessels and capillaries (Fig. 260 B_1).

The membranes overlying an old patch of softening are usually hyperplastic (C_1), the blood-vessels also often showing signs of thickening (f). A certain amount of cellular infiltration takes place not only into the walls of the cyst but also into the soft membranes (pia mater and subarachnoid), and this may continue as long as the process of disintegration goes on. Calcareous concretions are not infrequently formed in the thickened membranes, and the ganglion-cells in the parts contiguous to the cyst may also become calcified. When a patch of softening lies near a ventricle the latter usually becomes dilated by the falling away of its walls in the direction of the cyst of disintegration.

Ischæmic softening occurs at all parts of the central nervous system: in the brain the process is named briefly **encephalomalacia,** in the cord it has been called **myelomalacia.**

Softening of the cold affects the gray matter, the white matter, or

both together. It is interesting to observe that the anterior horns are more liable than other regions to undergo anæmic and hæmorrhagic softening: the anterior horn corresponds almost exactly with the vascular territory of one of the arterial twigs entering by the anterior longitudinal fissure, and when the circulation in it is suspended almost all the motor ganglion-cells in the corresponding half of the spinal segment must suffer.

Any part of the basal region of the brain may be the seat of softening, and the disorders of function thus induced are of the most various kinds. Occurring anywhere in the pyramidal (or motor) tract it leads to motor paralysis which is usually unilateral (hemiplegia): in the neighborhood of the bulbar nuclei or the conducting paths leading from them it gives rise to paralysis of one or more of the cranial nerves.

In the cerebrum softening occurs in the territory of the basilar or of the cortical arteries. Destruction of cortical centres thus brought about results in various motor and sensory paralyses. Thus destruction of the angular gyrus and occipital lobe implies loss of vision, destruction of the central convolutions and parietal lobe causes paralysis of the limbs on the opposite side, destruction of the left inferior-frontal convolution in right-handed persons induces motor aphasia, and so on. If the number of patches of cortical softening (Fig. 260) be great, all the functions of the brain may be more or less impaired.

Large and single or small and multiple softening occurring in the corona radiata or internal capsule lead to interruption of the motor tract and consequently to motor paralysis.

Localized softening in the anterior horns of the cord is followed by paralysis of special groups of muscles. Thus in a recent case observed by the author the muscles of one arm were paralyzed, in another one arm and the diaphragm; on examination patches of softening were in each case found in the anterior horn of the middle and lower portions of the cervical cord on the same side. Such ischæmic softenings of the anterior horns are frequently misdescribed by clinical observers as due to anterior poliomyelitis. EHRLICH and BRIEGER (*Zeitschr. f. klin. Med.* 1884) found that after temporary ligature of the aorta, by which the lumbar cord was deprived of blood for half an hour, the gray matter and the anterior roots were completely degenerated, the white columns still remaining intact.

644. **Softening from compression.** When the substance of the brain or cord is in any way subjected to severe compression, degeneration of the compressed tissue sooner or later sets in. Such compression is most frequent in the case of the cord, every encroachment on the narrow spinal canal involving almost of necessity a pressure on the soft tissue which it cannot escape. For example, tuberculous granulations, caseous matter and pus collecting in the epidural space during inflammatory disease of the vertebræ, tumors of the bone, dura mater, or pia mater, hæmorrhagic effusion into the membranes, varicosities or angiomatous

overgrowth of the pial vessels, dilatations of the central canal of the cord itself, dislocation of the vertebræ such as occurs in caries of the spine, all give rise to compression of the nerve-substance.

Loosening or rupture of the ligaments connecting the axis and atlas, such as occurs in carious disease of the upper cervical spine or occiput, or a blow on the back of the head or neck, may cause the odontoid process of the axis to press upon the medulla oblongata.

The injurious effect of sudden or gradual compression of the cord, apart from any mechanical damage of the tissues, is doubtless due in great measure to disturbance of the circulation, leading to more or less protracted anæmia of the nerve-substance. When this reaches a certain degree of intensity and duration anæmic necrosis and softening are induced. In like manner if the outflow of blood be hindered by the compression we have hæmorrhage from venous engorgement. The white matter is the first to soften; the gray matter usually persists for a time, its blood-supply being derived not from the periphery but from the vessels of the longitudinal fissures. According to KAHLER six hours after compression the axis-cylinders begin to swell up to such a degree that they sometimes seem to distend and stretch the meshes of the neuroglia. After the second day they begin to disintegrate, often becoming vacuolated in the process.

In the first week or two after compression the substance of the cord is white and opaque owing to the quantity of nerve-detritus which is present. Then it becomes more translucent, and at length gray and gelatinous, as the products of disintegration are absorbed. At the same time hyperplasia of the neuroglia sets in, and continues for some months, until the tissue is very considerably increased in amount and in density (Art. 639, Fig. 256). If the hæmorrhage has taken place during the process of softening the gray sclerotic tissue is more or less visibly pigmented.

Compression of the brain differs in its conditions from that of the cord much as the cranial cavity differs from the spinal canal. Thus if a meningeal tumor slowly encroaches on the space within the cranial cavity room is made for it by an efflux of lymph or cerebrospinal liquid from the brain, the latter so far altering its form as to become indented where the growth presses on it. The brain-substance remains uninjured unless the tumor is of considerable size: in this case it may cause a localized simple or degenerative atrophy. Degeneration is more common in cases of tumor growing within the brain, or of chronic cerebral abscesses, which by pressure on the sound tissue give rise to disturbance of the circulation.

Sudden encroachments are apt to damage the brain-substance, such for instance as are caused by hæmorrhages, or inflammatory exudations into the meninges or ventricles. Even sudden congestive hyperæmia may give rise to dangerous intracranial pressure.

Increased afflux of blood to the brain, inflammatory exudations, and hæmorrhagic effusions determine in the first instance an outflow of cerebrospinal liquid from the cranium into the spinal canal: sometimes indeed the liquid displaced is so abundant that the intervertebral ligaments bulge under its pressure. When however the intracranial pressure reaches a certain point no further displacement can take place, the capillaries of the brain are compressed, the circulation comes to a standstill, and the impaired nutrition of the nerve-elements results in impairment of their functions. If the pressure is not quickly relaxed by re-absorption of the effusion or by efflux of blood, so that the circulation is restored, and death does not at once ensue, extensive degenerative changes may take place in the parts first compressed. In remoter parts the pressure relaxes as the first give way. Thus it is very common to find a zone of softening immediately surrounding an extravasation of blood or an effusion into a ventricle, but not extending to any great distance.

References:—ERB, *Ziemssen's Cyclopædia* XIII.; LEYDEN, *Klinik d. Rückenmarkskrankh.* 1874–76; KAHLER and PICK, *Arch. f. Psych.* X.; CHARCOT, *Diseases of the nervous system* II. London 1880, *Gaz. méd.* 1874; BOUCHARD, *Dict. ency. d. sciences méd.* (second series) VIII; MICHAUD, *Sur la myélite et la méningite dans les mal. vertébr.* Paris 1871; BERGMANN, *Deutsche Chirurgie* part 30, 1880; KAHLER, *Prag. Zeitschr. f. Heilk.* III.; ADAMKIEWICZ, *Wien. Sitzungsber.* XLVIII. 1883, *Wiener Klinik* VIII., IX. (1884); WERNICKE, *Fortschritte d. Med.* III. 1885.

KAHLER experimented on compression of the cord by injecting melted wax into the spinal canal. Sclerosis resulted only after several months.

645. **Softening from contusion and concussion.** When the substance of the brain or cord is contused or crushed, or even violently shaken, it frequently undergoes complete and rapid necrosis and ultimately disintegrates.

A moderately abundant spontaneous hæmorrhage may have this effect, but among mechanical causes the commonest are dislocation and fracture of the vertebræ, blows or falls on the head (concussion), cuts or stabs penetrating the bony coverings of brain or cord, and projectiles reaching the central nervous tissues. Splinters of bone, such for example as occur in depressed fracture of the skull, should also be included.

The death of the nerve-substance is doubtless due to the direct injury to its elements and the rupture of their connections, and in part to the disturbance of the circulation and consequent failure of nutrition.

When the injury is very extensive it may speedily result in death. Where the contusion is less severe, as in the case of a blow on the head, the part directly injured or even the entire brain is the seat of capillary hæmorrhage, so that on section its appears mottled or speckled with spots of red. Extreme violence may cause immediate disintegration of the tissue, so that it becomes a mere mass of *débris* and blood. Meningeal hæmorrhage is an almost invariable accompaniment.

The changes resulting from traumatic destruction of the nervous tissues, provided septic inflammation is excluded, exhibit the characters partly of anæmic and partly of hæmorrhagic necrosis. Liquefaction and absorption of the products of disintegration ensue, the process not being essentially different from that described in connection with ischæmic necrosis, though the subsequent inflammatory changes are apt to be somewhat more intense than in the latter case (Art. 658). If the traumatic softening is confined to the cortex of the brain, we find some time afterwards defects in the convolutions, which are covered over by a mass consisting of collapsed capillaries, unabsorbed detritus, and granule-cells. Sometimes sclerotic thickening of the underlying brain-tissue takes place.

It is worth remarking that the degenerative changes set up by traumatic violence such as we have just described occasionally go on for years after the initial injury, and that a gradually advancing disintegration of the borders of the softened region takes place, by which in the course of time a very extensive destruction of tissue is effected. Thus for example after a blow on the forehead the whole of the frontal lobe may perish. Probably this progressive destruction depends on some secondary disease of the blood-vessels or obstruction of the lymphatics, which gives rise to permanent disorder of circulation and nutrition.

If the effect of the initial injury is slight there may be no general disintegration of tissue, the damage perhaps not extending beyond the necrosis and calcification of a few ganglion-cells.

The changes in the cord are exactly similar to those in the brain under the same conditions (Art. 659).

The clinical symptoms of concussion of the brain and cord (*commotio cerebri et medullæ spinalis*), namely partial or total loss of consciousness, confusion of mind, muscular weakness, disorder of the functions of the cord, etc., are not dependent on the local damage alone. Even in rapidly fatal cases this damage may be but slight. There is in fact a disturbance of the functions of the entire organ, due doubtless to the mechanical shock which affects detrimentally the whole of the nerve-substance (KOCH, FILEHNE, WITKOWSKI, BERGMANN).

In infants who die soon after birth we often meet with subdural and intra-meningeal hæmorrhages, due no doubt to rupture of the venous sinuses or sub-arachnoid veins from displacement and compression of the cranial bones in the act of parturition.

Workmen engaged in bridge-building and exposed to high air-pressure in sunken caissons are sometimes seized with paralysis when they come out suddenly into the free air. LEYDEN (*Arch. f. Psych.* IX.) found in some of them small patches of degeneration in the cord. These he attributes to the rapid escape of gas (oxygen) from the blood, which had under high pressure absorbed it in excess, the bubbles probably forming small emboli in the vessels.

References:—BERGMANN, *Kopfverletzungen, Deutsche Chirurgie* part 30, 1880; FISCHER, *Sammlung klin. Vorträge* 10, 27; BRUZELIUS and KEY, *Virchow's Jahresber.* II. (1880); FRONMÜLLER, *Die Rückenmarkszerreissung, Memorabilien* 1876; W. MÜLLER, *Path. Anat. u. Physiol. d. Rückenmarks* Leipzig 1871; ERB,

Ziemssen's Cyclopædia XIII.; CLEMENS, *Die Erschütterung d. Rückenmarks, Deutsche Klinik* 1863-65; OBERSTEINER, *Wiener med. Jahrb.* 1879; VON RECKLINGHAUSEN, *Virch. Arch.* vol. 30; JOLLY, *Stud. a. d. Inst. f. exp. Path.* Vienna 1870; KRAFFT-EBING, *Die d. Gehirnerschütt. u. Kopfverletzungen hervorgerufenen psych. Krankh.* Erlangen 1868; KOCH and FILEHNE, *Langenbeck's Arch.* XVII. (1874); WITKOWSKI, *Virch. Arch.* vol. 69.

646. **Secondary degeneration of the tracts** (systemic degenerations). Destruction of certain parts of the brain and cord is followed by a degeneration of certain corresponding tracts of nerve-fibres, which is called secondary degeneration. It is probably due to the fact that the affected tracts are severed from their 'trophic centres,' or that these latter are destroyed. We have ascending and descending secondary degeneration, according to the direction in which the process advances.

Descending degeneration is commonest in the pyramidal tracts (Art. 626, Fig. 246 *Pvb Psb*), and takes place in all cases in which the motor centres of the cerebral cortex are destroyed, or in which the motor tract as it passes through the corona radiata, the internal capsule, the peduncular region, or the pyramidal columns, is anywhere interrupted. The degeneration extends down to the points at which the motor fibres leave the anterior horns of the cord. In rare cases the ganglion-cells of the anterior horns also are atrophied, and then the motor fibres in the anterior roots of the spinal nerves become degenerate. When the destruction of the cortical centres is incomplete or only superficial it is not usually followed by secondary degeneration. It must however be borne in mind that in insane paralytic patients, in whom extensive superficial atrophy of the motor region of the cortex has resulted from chronic inflammation, we meet with degeneration of the pyramidal tract: this is however probably a secondary disease of the cord rather than a secondary degeneration in the strict sense of the term (Art. 647).

When the primary disease is in the cord, and such that the motor tract is entirely interrupted, the anterior pyramidal tract below the affected section becomes atrophied, but only for a distance of one or two centimetres, a few fibres perhaps showing degenerative change for a greater distance. In the case of the posterior columns of Burdach the degeneration extends downward along some fibres as much as six centimetres. The latter are perhaps fibres which enter with the posterior roots and then pass downwards for a certain distance in the substance of the cord (SCHULTZE).

According to CHARCOT when the anterior portion of the internal capsule is destroyed secondary degeneration appears in a bundle of fibres passing through the middle of the crustal stratum of the crus to the pons and probably ending in some of the nuclei of the medulla.

Ascending degeneration follows upon destruction of the cord or of the posterior root-fibres of the spinal nerves.

If the cord is cut across all the posterior tracts degenerate for a short

distance above the point of section, the columns of Goll (Fig. 246 *fgr*) alone degenerate for a greater distance, namely up to the nucleus of the funiculus gracilis. Destruction of the posterior roots has the like effect. It is thus rendered probable that the columns of Goll have their trophic centre in the spinal ganglion-cells.

If the cord is cut in the upper dorsal region the direct cerebellar tracts (Fig. 246 *Ksb*) above the lesion become degenerate: they pass from the vesicular columns (of Clarke) to the cerebellum. According to SCHULTZE a small region of the lateral column near the periphery also undergoes atrophy.

Secondary degeneration occurs chiefly after ischæmic softening, atrophy from compression, and hæmorrhagic or inflammatory destruction of the tracts and centres indicated. It does not always follow upon sclerosis of the cord or brain, inasmuch as the conducting tracts are apparently not always entirely interrupted in passing through sclerotic patches.

The degeneration takes place simultaneously over the whole extent of the affected tract. It is recognizable under the microscope in the second week after the initial lesion, disintegration of the medullary sheath and axis-cylinder of the nerve-fibres having by that time begun. When it has advanced to a certain point absorption of the products of disintegration begins, and the familiar granule-cells make their appearance. The space vacated by the atrophied fibres is filled up partly by effusion of liquid, partly by hyperplasia of the neuroglia, though it may be months or years before the latter becomes fairly dense and compact (Art. 639, Figs. 255, 256).

So long as the degenerate tracts contain abundance of detritus they are white, opaque, and soft. As absorption goes on they become gray and translucent; when sclerosis takes place they become firm, and at the same time shrink in volume.

In the text we have spoken only of total secondary degeneration of the longitudinal tracts of the brain and cord. Of course particular bundles of fibres may likewise undergo degeneration, and even the short transverse or commissural fibres of the cord. SCHULTZE met with a case of traumatic injury to the sciatic fibres in the lumbar cord, in which only the posterior portions of the columns of Goll were atrophied. Nerve-tracts degenerate from the initial lesion up to the next terminal organ, and apparently in the direction of normal conduction. Some of the fibres of the cord however do not degenerate in either direction after an interrupting lesion (FLECHSIG).

BOUCHARD and SCHIEFFERDECKER found secondary degeneration 14 days after lesion, W. MÜLLER 13 days, and KAHLER and PICK 11 days.

References:—TÜRCK, *Zeitschr. d. Gesell. d. Aerzte in Wien* 1850, *Wiener Sitzungsber.* VI. (1851), XI. (1853); WALLER, *Müller's Arch.* 1852: WESTPHAL *Arch. f. Psych.* II.; SIMON, *ibid.* V.; LEYDEN, *Deutsche Klinik* 1863, *Klin. d. Rückenmarkskr.* II.; BOUCHARD, *Arch. générales* 1866; GUDDEN, *Arch. f. Psych.* II. (1869); CHARCOT, *Diseases of the nervous system* London 1878–80, *Leçons sur la localis. dans les mal. d. cerveau* I. Paris 1878–80, *Progrès méd.* 1879; FLECHSIG-

Die Leitungsbahnen Leipzig 1876, *Arch. d. Heilk.* XVIII. (1877), *Ueber Systemerkrankungen* Leipzig 1878; SCHULTZE, *Cent. f. med. Wiss.* 1876; *Virch. Arch.* vol. 79, *Arch. f. Psych.* XIII., XIV.; MEYER, *ibid.* XIII.; KAHLER and PICK, *ibid.* X.; BINSWANGER, *ibid.* XI.; SCHIEFFERDECKER, *Virch. Arch.* vol. 67; HAYEM, *Arch. de physiol.* V (1873); HOMÉN, *Virch. Arch.* vol. 88, *Fortschritte d. Med.* III. (1885); ERB, *Ziemssen's Cyclopædia* XIII.; NEELSEN, *D. Arch. f. klin. Med.* XXIV. (1879); FERRIER, *Localization of cerebral disease* London 1878, *Trans internat. med. congress* I. London 1881; BRAMWELL, *Diseases of the spinal cord* Edinburgh 1884; BARTH, *Arch. d. Heilk.* X.; MÜLLER, *Path. Anat. d. Rückenm.* 1871; ISARTIER, *Des dégén. second. de la moëlle épin. conséc. aux lésions du cerveau* Paris 1878; LÖWENTHAL, *Fortschritte d. Med.* I. (1883); MENDEL, *Neurolog. Centralb.* I. (1882); MARTINOTTI, *Sulle degen. sistem. del midollo spin. second.*, *Collezione ital. di medicina* (3d series) 11 and 12, 1885; LANGLEY, *Brain* VIII. 1886.

647. **Primary scleroses of the columns of the cord.** Primary sclerosis or gray degeneration is a change extending over entire tracts or columns of the spinal cord: it resembles secondary degeneration in its course and results, differing from it however in the apparent absence of any interrupting lesion of the conducting paths.

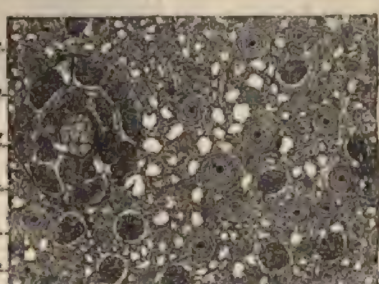

FIG. 261. SCLEROSIS OF THE POSTERIOR WHITE COLUMNS OF THE CORD.
(*Section treated with Müller's fluid, hæmatoxylin, carmine, and perosmic acid, and mounted in glycerine:* × 150.)

a, section of normal nerve-fibres
b, granule-cells
c, neuroglia with nuclei
d, blood-vessel
e, granule-cells in the lymph-sheath of the vessel *d*

Its essential characters are degeneration of the nerve-fibres and hyperplasia of the connective tissue (sclerosis), but the relations of these are somewhat different from those observed in secondary degeneration. Disintegration of the nerve-elements and increase of the neuroglia begin almost simultaneously and go on side by side: indeed some have regarded the neurogliar hyperplasia as the primary disorder and the degeneration of nerve substance as secondary to it. There is however no real doubt that the degeneration is the primary and essential feature of the disease.

The medullary sheaths are the first to disintegrate, and then the axis-cylinders; the degenerating tract thus loses in succession a number of its fibres, greater or less according to the duration of the affection

(Fig. 261). Fat-granule cells (*b e*) appear, as in all nerve degenerations, and accumulating chiefly in the lymph-sheaths (*d*) of the vessels are carried off by these channels. While this is going on the cells of the neuroglia (*c*) begin to multiply, and as the nerve elements dwindle and disappear the connective tissue increases and fills their places. Thickening of the vessel-walls also takes place.

Sclerosis is commonest in the posterior columns of the cord, and is the anatomical basis of the disease known as **tabes dorsalis** or locomotor ataxy.

FIG. 262.

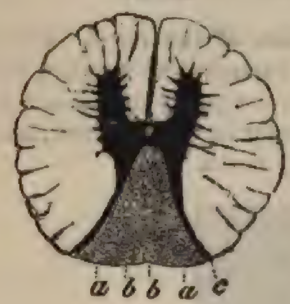

FIG. 263.

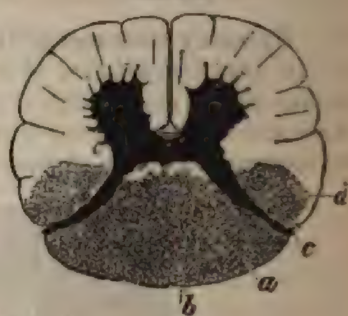

FIG. 264.

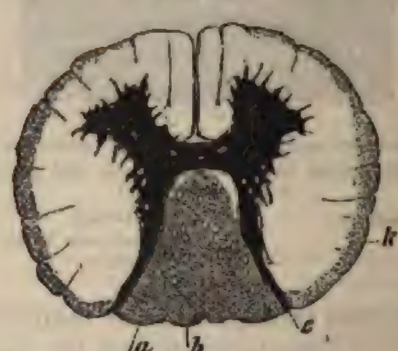

FIG. 262. COMPLETE SCLEROSIS OF POSTERIOR COLUMNS AND ATROPHY OF POSTERIOR ROOTS.

(*Section through dorsal region*: × 5.)

a, cuneate fasciculus
b, column of Goll
c, atrophied posterior root

FIG. 263. SCLEROSIS OF POSTERIOR AND LATERAL COLUMNS.

(*Section through upper lumbar region*: × 5.)

a, cuneate fasciculus
b, column of Goll
c, atrophied posterior root
d, posterior portion of lateral column

FIG. 264. SCLEROSIS OF POSTERIOR COLUMNS AND OF MARGINAL REGION.

(*After* WESTPHAL: *section through cervical region*: × 5.)

a, cuneate fasciculus
b, column of Goll
k, marginal sclerosis along direct (or lateral) cerebellar tract

In advanced cases the degeneration and sclerosis may extend over the entire section of the posterior columns in the dorsal region of the cord (Fig. 262). In the lumbar region (Fig. 263) the anterior portion of the section is almost always exempt. In the cervical region (Fig. 264) two lateral segments of the anterior portion are spared or but slightly affected. The changes are usually (unless the degeneration is universal) most marked in the lumbar and dorsal regions, though cases occur in which the cervical region is the most affected. The degeneration ascends within the columns to beyond the obex of the calamus scriptorius and ceases about the level of the *striæ acusticæ* (Fig. 248, Art. 629).

When the degeneration of the posterior columns is well-advanced their outer surface assumes a gray or grayish-red tint, and on section the tissue appears quite gray and translucent. At the same time the columns appear somewhat shrunken.

The posterior nerve roots are always more or less atrophic and gray, the atrophy being greatest when the general degeneration is most advanced. The posterior root-fibres within the cord are likewise atrophic; and not alone those which pass forward through the substance of the posterior columns but also those which traverse the posterior root-zones. In rare cases some of the ganglion cells of the gray matter are destroyed.

This degeneration of the posterior columns with the accompanying changes in the posterior roots is usually an independent and uncomplicated malady: but cases occur in which simultaneously or subsequently portions of the lateral columns also undergo degeneration (Fig. 263 *d*).

The portions most apt to be invaded are the posterior (pyramidal tracts) and the marginal (direct cerebellar tracts, Fig. 264 *k*): sometimes the marginal sclerosis extends right round to the anterior columns.

A second form of primary degeneration is that known as **amyotrophic lateral sclerosis.** It is essentially a degeneration of the lateral columns extending over the whole length of the cord, and accompanied by atrophy of the ganglion-cells of the anterior horns and the equivalent gray nuclei in the medulla.

The degeneration of the white matter is marked by atrophy, disintegration, and disappearance of nerve fibres, together with increase of connective tissue, though the sclerotic induration is not usually so extreme as in the corresponding affection of the posterior columns. Only when the disease has lasted a very long time the new fibrous tissue become dense and compact.

In many cases the degeneration is limited to the lateral pyramidal tracts (Fig. 265 *b*): and thus where these tracts have a well-marked contour on section, namely in the cervical region, the disease is also sharply defined; where they are interpenetrated by other systems of fibres and extend forwards, as in the dorsal region, it is difficult to make

out the exact extent of the disease. If the pyramidal tracts have decussated completely at the medulla, the degeneration is confined to the lateral columns (Fig. 265 *b*); but if some of the strands are undecussated then the anterior (or uncrossed) pyramidal tracts are also affected. In other cases again the short tracts in the anterior-lateral columns variously described as principal tracts (FLECHSIG) and anterior root-zones (CHARCOT) undergo a like change. These tracts connect the various segments of the cord with each other and with the medulla, and include root-fibres which run longitudinally for a certain distance within the cord before passing out with the roots.

The direct cerebellar tracts are invariably exempt. In an ascending direction the disease has been traced up to the pons and crura cerebri, but no further. We are thus ignorant of the upper limit of the change, and it is quite possible that it sometimes extends up to the cortex.

FIG. 265. AMYOTROPHIC LATERAL SCLEROSIS.

(*Section through the cervical cord:* × 10.)

a, anterior horns, the ganglion-cells of which have almost all disappeared
b, diseased region of the lateral column corresponding to the completely decussated pyramidal tract

In the anterior horns it is chiefly the most anterior ganglion-cells which perish (Fig. 265 *a*); those of the intermedio-lateral tract are scarcely if at all affected; while those of Clarke's columns are quite exempt.

Of the motor nuclei of the cerebral axis those of the hypoglossal, facial, and spinal accessory nerves are the most liable to atrophic change; and to a very much less extent those of the abducens and trigeminal nerves. Details regarding the limits to which the atrophy may extend are unfortunately lacking.

In proportion to the atrophy of the motor ganglion-cells in the cord

and medulla we have of course progressive atrophy of the corresponding motor nerves and muscles.

Amyotrophic lateral sclerosis is from a pathological point of view closely akin to anterior poliomyelitis, or spinal paralysis with wasting of the ganglion-cells in the anterior horns (Arts. 640, 659).

CHARCOT, ERB (*Virch. Arch.* vol. 70), and others incline to the belief that a primary form of sclerosis of the pyramidal tracts exists, unaccompanied by degeneration of the anterior horns, and giving rise to a group of symptoms described by ERB as spastic spinal paralysis, by BERGER as **primary lateral sclerosis,** and by CHARCOT as spasmodic tabes dorsalis. STOFFELA (*Wien. med. Woch.* 21, 1878) describes a case of sclerosis of the lateral columns only, but the anatomical examination was not sufficiently minute to prove that it was a primary lateral sclerosis. The like is true of the older instance given by TÜRCK (*Wiener Sitzungsber.* XXI. 1856). Probably it was a case of amyotrophic lateral sclerosis. See however DRESCHFELD, *Journ. of Anat. and Physiol.* XV. 1881, and the cases and references given by ROSS, *Diseases of the nervous system* II. London 1883. The author's experience induces him to agree with LEYDEN (*Berl. klin. Woch.* 48, 1878), SCHULZ (*D. Arch. f. klin. Med.* XXIII.), WEISS (*Wien. med. Woch.* 1883), and STRÜMPELL (*Arch. f. Psych.* X.), in their view that the symptoms of spastic spinal paralysis may be caused by disseminated sclerosis, myelitis, degeneration from compression, tumors, spinal meningitis, hydromyelia, etc. The nature of the lateral sclerosis of chronic insane paralytic patients (WESTPHAL, *Virch. Arch.* vol. 40; SCHULTZE. *Arch. f. Psych.* IX.) is still in dispute: FLECHSIG regards it as a secondary degeneration, WESTPHAL as a primary affection.

References on the morbid anatomy of tabes dorsalis:—LEYDEN, *Die graue Degen. d. hint. Rückenmarksstränge* Berlin 1863, *Klinik d. Rückenmarkskr.* II., *D. Zeitschr. f. klin. Med.* 1877, Art. *Tabes dorsalis* in *Realencyclop. d. gesammt. Heilkunde;* PIERRET, *Arch. d. physiol.* III. (1870), IV., V., *Les symptomes céphaliques du tabes dorsalis* Paris 1876, *Gaz. méd. de Paris* 1882; FROMMANN, *Unters. üb. norm. u. path. Anat. d. Rückenmarks* Jena 1867; RINDFLEISCH, *Path. Histology* II. London 1873; SOLLY and CLARKE, *St. Thos. Hosp. Reports* 1870; WESTPHAL, *Arch. f. Psych.* V., IX., XII., XVI.; WOLFF, *ibid.* XII.; ADAMKIEWICZ, *ibid.* IX., X. XII., *Trans. internat. med. congress* II. London 1881, *Die Rückenmarksschwindsucht* Vienna 1885; TAKACS, *Cent. f. med. Wiss.* 1878, *Arch. f. Psych.* IX.; CHARCOT, *Diseases of the nervous system* London 1876–80; VULPIAN, *Maladies du système nerveux* Paris 1879; SIMS WOODHEAD, *Journ. of Anat. and Physiol.* XIV. (1882); ERB, *Ziemssen's Cyclopædia* XIII.; FRIEDREICH, *Virch. Arch.* vols. 26, 27, 68, 70; STRÜMPELL, *Naturforscherversammlung in Salzburg* 1881, *Arch. f. Psych.* XII. (1882) (and *Brain* V. 1882); JÄDERHOLM, *Nord. med. Arkiv.* I.; KAHLER, *Zeitschr. f. Heilk.* II. (1882); RAYMOND and ARTAUD, *Soc. de biol.* July 1882; ROSS, *Diseases of the nervous system* II. London 1883 (with numerous references); BRAMWELL, *Diseases of the spinal cord* Edinburgh 1884 (for good figures); BUZZARD, *Brain* VI. 1884 (disease of blood-vessels); KRAUS, *Neurolog. Centralb.* 1885; DÉJÉRINE, *Arch. de physiol.* 1884; BABINSKI, *ibid.* 1885; LISSAUER, *Fortschritte d. Med.* III. 1885.

References on amyotrophic lateral sclerosis and bulbar paralysis:—DUCHENNE, *Gaz. hebdom.* 1859, 1861; CHARCOT, *Diseases of the nervous system* II. London 1880; FLECHSIG, *Ueber Systemerkrankungen* Leipzig 1878; BARTH, *Arch. d. Heilk.* XII., XV.; DUMÉNIL, *Gaz. hebdom.* 1867; LEYDEN, *op. cit.*, *Arch. f. Psych.* II., III., VIII.; MAIER and KUSSMAUL, *Virch. Arch.* vol. 61; GOMBAULT, *Arch. de*

physiol. IV.; PICK, *Arch. f. Psych.* VIII.; PITRES, *Arch. de physiol.* 1876; LÉPINE, *Gaz. méd. de Paris* 17, 1878; WESTPHAL, *Virch. Arch.* vol. 40; KUSSMAUL, *Sammlung klin. Vorträge* 54; WORMS, *Arch. de physiol.* IV. (1877); CORNIL and LÉPINE, *Gaz. méd. de Paris* 1875; FERRIER, *Lancet* 1, 1881; STADELMANN, *D. Arch. f. klin. Med.* XXXIII.; MOELI, *Arch. f. Psych.* X.; VIERORDT, *ibid.* XIV.; DÉJÉRINE, *Arch. de physiol.* VI. (1883); MINKOWSKI, *D. Arch. f. klin. Med.* XXIV. (1884); ORMEROD, *Brain*, VIII. 1886 (a critical digest).

On sclerosis affecting more than one tract ('combined degeneration'):—WESTPHAL, *Virch. Arch.* vols. 39, 40, *Arch. f. Psych.* V., VIII., IX. XV. (causation of spastic spinal paralysis); KAHLER and PICK, *ibid.* VIII., X.; SCHULTZE, *Virch. Arch.* vol. 79, *Arch. f. Psych.* V.; FRIEDREICH, *Virch. Arch.* vols. 26, 27, 68, 70; STRÜMPELL, *Arch. f. Psych.* XI.; PRÉVOST, *Arch. de physiol.* IV. (1877); WOLFF, *Arch. f. Psych.* XII.; HAMILTON, *New York med. record* XV. (1879); BABESIU, *Virch. Arch.* vol. 76; ORMEROD, *Brain* VII. 1885 (a critical digest of the literature).

648. From what we have said in the last Article it will be seen that both in tabes dorsalis and in amyotrophic lateral sclerosis the morbid change follows the course of certain definite tracts, and the question at once arises whether in these cases we have what with FLECHSIG we may call **primary systemic diseases.** If by a 'system' we mean one definite group of homologous nerve-fibres and their ganglion-cells, and this only, these affections can hardly be described as simply 'systemic,' inasmuch as at least in tabes various systems are involved. Tabes would in that case be properly described as a combined systemic disease (STRÜMPELL). But if we include under the term 'system' a group of fibres and cells all *functionally* related, both tabes and amyotrophic lateral sclerosis are systemic.

The **morbid change in tabes** has been variously interpreted by different authors. LEYDEN regards it as a degenerative process, CYON, FRIEDREICH, and FROMMANN regard it as inflammatory, CHARCOT calls it a parenchymatous inflammation, ERB a chronic myelitis. ADAMKIEWICZ thinks the essential fact is a chronic degeneration of the connective tissue.

Minute microscopic examination shows however that the process is essentially a degenerative one, having nothing to do with inflammation: and STRÜMPELL accurately expresses the facts when he describes it as a degeneration of functionally related nerve-fibres.

According to PIERRET, CHARCOT, and STRÜMPELL the disease begins with the degeneration of certain strands of fibres running through the middle of Burdach's columns (Fig. 266 *a*), and usually in the lumbar and dorsal regions of the cord. At the same time degenerate fibres appear in the posterior nerve-roots, and along the inner (or median) aspect of Goll's columns in the dorsal and cervical regions there is a sclerotic strip. After a time Burdach's columns in the cervical region are likewise invaded.

We have thus at first patches and strips of degeneration occurring in centripetal fibres which enter the cord through the posterior roots. This

is followed by secondary ascending degeneration of the fibres initially attacked in the lower part of their course. Tabes according to this view then is a localized multiple ascending degeneration primarily affecting a part of the region of the posterior columns, which with its associated secondary degenerations extends in the course of years over nearly the whole of that region.

As to the **cause** of the first onset of the affection—whether it depends on some congenital or acquired weakness of the centripetal tracts, or on disordered nutrition from disturbance of the circulation—it is not easy to decide. The fact that some forms of tabes appear to be inherited or at least congenital (FRIEDREICH) supports the former supposition, while the latter agrees with the observation that very frequently we find almost from the commencement of the disease like disorder of the optic, oculomotor, and trigeminal nerves, while simultaneously with its progress multiple patches of sclerosis appear in other parts of the brain and

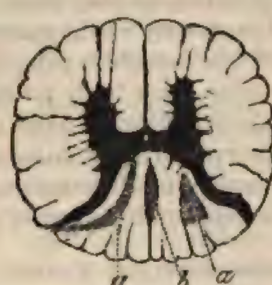

FIG. 266. COMMENCING SCLEROSIS OF THE POSTERIOR COLUMNS.

(*After CHARCOT: section from the dorsal region*: × 5.)

a, sclerotic patch in the cuneate fasciculus *b*, sclerotic patch in the columns of Goll

cord. When simultaneous degeneration of other systems of fibres takes place we can only suppose that the like weakness of organization or disorder of nutrition is affecting them also. At least there is no ground for the theory that the imagined inflammatory process has extended by continuity from the primarily diseased posterior columns to other tracts.

At present we cannot say anything as to the real nature of the exciting cause. Clinical observers mention a great variety of predisposing conditions, such as cold, over-exertion, sexual excess, etc. FOURNIER, ERB, GOWERS, and others have lately laid special stress on **syphilis** as the commonest of all antecedents of tabes. If when the pathogenic agency is extrinsic the sensory tracts alone are affected, we must assume either that they have been congenitally weaker than the others, or that they are normally less able to resist certain forms of injury.

The like difficulties arise in the case of amyotrophic lateral sclerosis. Here also we are driven to conclude that the disease is a result of a

localized degeneration occurring primarily in the region of the motor tract, perhaps also in the motor nuclei, and followed by a secondary degeneration along the course of the pyramidal fibres. This is the more likely inasmuch as the degeneration of the pyramidal tracts is most marked and typical when the degeneration affects chiefly the medulla oblongata; while a like degeneration beginning in the gray matter of the lumbar cord is not as a rule followed by any appreciable change in the pyramidal tracts (Art. 640). In some cases indeed (ZIEGLER) the medulla shows not only atrophy of the ganglion-cells of the gray nuclei but also patches of softening in the white matter of the pyramids: descending secondary degeneration may well start from the latter also.

When portions of the white matter of the anterior root-zones and neighboring lateral regions are affected as well as the pyramidal tracts, we may explain the apparent complication by assuming that fibres belonging to the anterior (uncrossed) pyramidal tracts run through the anterior root-zones (FLECHSIG), as they they sometimes do; while we also bear in mind that the atrophy of the ganglion-cells of the anterior horns involves atrophy of the root-fibres entering and leaving the white substance. Perhaps in some cases fresh primary foci of degeneration appear in the region of the commissural fibres of the anterior columns. And when as has been observed in a few instances the posterior columns are likewise affected, we must infer that there too some isolated patch of degeneration has led to secondary degeneration of the tract.

Many authors (FRIEDREICH, SCHULTZE, KAHLER, PICK) have asserted that defective development of the conducting columns is frequently the principal cause of primary systemic degeneration. In support of this they point to the fact that certain forms are hereditary (FRIEDREICH, *Virch. Arch.* vols. 68, 70; RÜTIMEYER, *ibid.* vol. 91; DRESCHFELD, *Liverpool and Manchester med. and surg. reports* IV. 1876; ORMEROD, *Brain* VII. 1884; EVERETT SMITH, *Boston med. and surg. journ.* 1885; BURY, *Brain*, VIII. 1886, with summary of cases), and that in these cases post-mortem examination has revealed changes explicable only on the supposition of imperfect development of the cord. It cannot be denied that in some cases hereditary conditions play a considerable part. In others, and these the majority, there is no evidence of such conditions, and we must look elsewhere for the causes of the disease. ERB (*D. Arch. f. klin. med.* XXIV. (1879) *Cent. f. med. Wiss.* 1881, *Trans internat. med. congress* II. 1881, *Berl. klin. Woch.* 32, 1883), FOURNIER (*L'ataxie locomotrice d'origine syphilitique* Paris 1882), GOWERS (*Lancet* 1, 1881), ALTHAUS (*Trans. internat. med. congress* II. 1881) VOIGT and KUMPF (*Berl. klin. Woch.* 1883), EULENBURG (*Virch. Arch.* vol. 99), and others have pointed out the great significance of syphilis in this connection, some going so far as to say that 80 to 90 per cent of tabic patients have suffered from syphilis. Even though other observers like WESTPHAL and BUZZARD have been unable to agree with such high estimates it appears plain that the influence of syphilis in the genesis of the disease is an important one.

ADAMKIEWICZ has carefully investigated the distribution of the blood-vessels in the cord (*Wiener Sitzungsber.* LXXXIV., LXXXV. 1882, XC. 1884) and shows that the degeneration of the posterior columns is coextensive with the vascular territory of the arteries which enter from the posterior circumference and the po-

terior longitudinal fissure. Even if we cannot suppose that all the vessels entering from these situations become successively diseased, we may at least imagine that the initial or primary lesion is due to disease within the territory of some of them, and that this lesion is the starting-point of secondary degeneration of the corresponding tracts. This at least would explain why the process sometimes does not extend over the whole of the posterior columns and the adjacent gray matter. On the other hand the fact that the disease of the posterior columns so often coexist with like disease of other systems and tracts shows that the degeneration may start in other vascular territories also.

TUCZEK (*Arch. f. Psych.* XIII.) states that in ergotism changes resembling those in tabes appear in the posterior columns: according to LEYDEN this is also the case in pellagra (Art. 369). BRUNELLI (*Trans. internat. med. congress* II. 1881) attributes an affection presenting the symptoms of lateral sclerosis to the use of bread contaminated with *Lathyrus cicera*. If these observations are confirmed in numerous cases they will go to show that certain poisons have a selective action on definite tracts of the central nervous system (ADRIANI, *La pellagra* Perugia 1880; ALTHAUS, *Brit. Med. Journ.* 1, 1884).

The fact that we occasionally meet with thickening of the meninges in tabes does not prove that the disease originally starts in meningitis. The thickening of the pia mater may quite well be a secondary process, though of course it is possible that it may be primary and give rise to the characteristic degenerative changes in the cord.

WESTPHAL (*Virch. Arch.* vols. 39, 40, and *Arch. f. Psych.* XII. 1882) and CLAUS (*Allg. Zeitschr. f. Psych.* XXXVIII. 1881) have shown that in patients suffering from paralytic dementia (general paralysis of the insane) gray degeneration or sclerosis of the posterior columns is very common. The inference is either that such patients are peculiarly liable to tabes, or that the exciting causes, which in the brain produce the changes that are manifested as progressive paralysis, are potent to give rise in the cord to gray degeneration. See STEWART, *Glasgow Med. Journ.* 1886.

DÉJÉRINE (*Soc. de biologie* Feb. 18, 1882, *Arch. de physiol.* 1883, *Comptes rendus* 1883) states, what had already been pointed out by FRIEDREICH and WESTPHAL, that in tabes the peripheral nerves undergo degeneration. He infers that the affection is primarily a peripheral one; but the facts afford no real ground for such a supposition. See also SAKAKY, *Arch. f. Psych.* XV.; OPPENHEIM and SIMMERLING, *Neurol. Centralb.* 11, 1886.

649. **Multiple sclerosis.** This is a peculiar affection of the brain and cord characterized by the formation of a number of gray condensed patches in the nervous tissues. It is either confined to the cord or extends over the whole of the central nervous system.

The patches are some of them superficial, some deep: in the former case they can be recognized by their gray color. Sometimes they are rounded in shape, sometimes elongated and irregular. Their diameter varies from 1 millimetre to 50 or more. On section they look uniformly gray and translucent, occasionally one or two are mottled with white and softer than the others. They are usually sharply-defined against the sound tissue, though now and then a patch is surrounded by an ill-defined zone of a grayish-white or mottled appearance. In general they are firm and dry, but cases occur in which they are softer than the healthy tissue and contain a quantity of liquid that escapes on section.

The dense patches (Fig. 267) consist of a close feltwork of delicate sharply-contoured fibres, beset with a larger or smaller number of nuclei. Within the larger and firmer patches no nerve fibres can be seen; in the smaller and more recent or round the border of the larger ones a few still persist (*a*): they are usually normal in appearance, though sometimes they show signs of degeneration. Fat-granule cells are in some cases entirely absent, though in general a few can be seen.

The vessels (*c*) are at times unaltered, in other cases their walls undergo a hyaline thickening or the adventitial coat is denser than usual. Sometimes too the adventitial lymph-sheaths contain lymphoid and granule-carrying cells, while leucocytes in varying number are scattered through the surrounding nerve-tissue.

Most of the nuclei that are visible belong however to the neuroglia-cells, which have a scanty protoplasm and a large number of glistening processes (Art. 638, Fig. 253). The feltwork is in fact essentially composed of the interlacing processes of these cells.

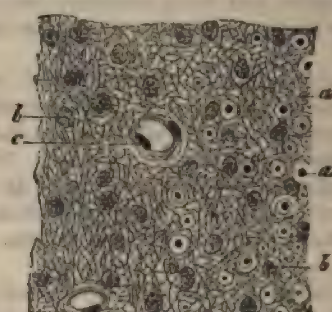

FIG. 267. SCLEROTIC PATCH IN THE WHITE MATTER OF THE CORD.

(*Section treated with Müller's fluid, alcohol, and carmine:* × 300.)

a, section of nerve-fibres
b, neuroglia-cells
c, blood-vessels

A few corpora amylacea occur here and there.

The softer and more gelatinous patches have a looser feltwork, with wider meshes and interstices. Those that are mottled with white contain numerous granule-cells and other products of nerve-disintegration. If they lie within the gray matter they sometimes contain also atrophied and shrunken or hyaline and swollen ganglion-cells.

The affection is commonest in the cord, and varies very greatly in its extent. There is nothing special about the manner in which the patches are distributed: they may lie anywhere in the gray matter as well as in the white (Figs. 268, 269, 270). When they interrupt conducting tracts, more or less extensive secondary degeneration of these ensues, but it is surprising to note how frequently the latter change is absent even when the sclerotic patches are pretty large. If the sclerosis should cause

the destruction of ganglion-cells in the anterior horns some of the anterior root-fibres of course become atrophied.

In the brain the chief seats of multiple sclerosis are the white matter near the lateral ventricles, the corpus callosum, the corpora striata, the pons, the crura cerebri, and the dentate nucleus. Often too the optic, olfactory, and trigeminal nerves, and the roots of the spinal nerves, are found diseased. In the case of the brain we now and then find that a large portion of the roof of the lateral ventricle is transformed into gray sclerotic tissue several millimetres thick. Multiple sclerosis of the cortex is comparatively rare.

650. In most cases when the gray patches of multiple sclerosis come under observation the tissue-change is well advanced, and appears to be due to increase of the neuroglia and consequent compression and atrophy of the nerve-elements. This late appearance gives us however no certain knowledge as to the origin and course of the affection. Even when the increase by hyperplasia of the connective tissue is the most obvious fea-

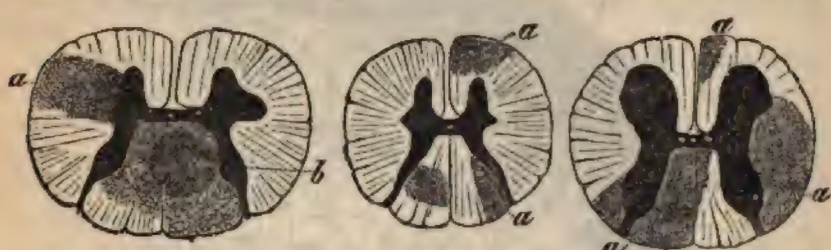

FIG. 268. FIG. 269. FIG. 270.

DIAGRAMS OF MULTIPLE SCLEROSIS (× 3).

FIG. 268. CERVICAL REGION.

a, sclerotic patch in the lateral column and left intermedio-lateral tract
b, patch in the posterior columns

FIG. 269. DORSAL REGION.

a, disseminated patches

FIG. 270. LUMBAR REGION

a, disseminated patches

ture in the ultimate result, it does not follow that the change began with such hyperplasia.

In fact there is no doubt that in many cases the disease begins as a degeneration, dependent primarily on a disturbance of nutrition, and first affecting the nerve-elements. Cases sometimes occur in which the typical gray sclerotic patches are accompanied in the brain and cord by others which are mottled with white, or uniformly white and opaque, or even pale-yellow; and these manifest on the one hand all grades of degenerative change, on the other an obvious proliferation and hyperplasia of the neuroglia (Art. 638, Fig. 253). In teased preparations we find not only abundance of nerve-detritus and granule-cells, but also numerous neuroglia-cells whose protoplasm is abundant and nuclei multiplied:

and as we have seen (Arts. 638, 639) there is no doubt that degenerative changes in the nerve-elements may be followed by multiplication of neuroglia-cells and formation of sclerotic patches.

The changes we are considering are certainly often of a non-inflammatory kind, being simply the results of disordered nutrition due to change or impurity in the blood, to thickening or degeneration of the vessel-walls, or to disturbance of the circulation. It is at any rate remarkable how frequently we find morbid changes in the vessel-walls in connection with sclerotic patches. Once however a sclerotic hyperplasia has begun it may extend to contiguous parts without any antecedent degeneration.

Though we are thus able in a number of cases to refer the sclerotic

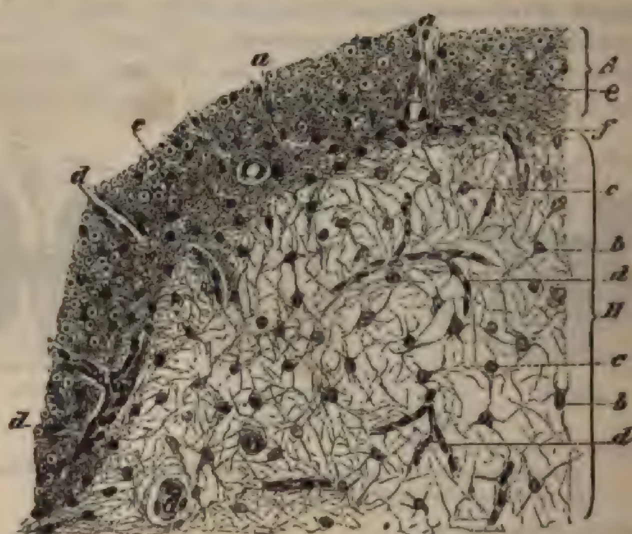

FIG. 271. GRAY GELATINOUS DEGENERATION OF THE ANTERIOR HORN.

(*From the lumbar cord*, 18 *months after an attack of acute poliomyelitis: prepared with Müller's fluid, hæmatoxylin and carmine, and Canada balsam:* × 200.)

A, white matter
a, atrophied anterior roots
b, branching neuroglia-cells forming a network of fine glistening fibres
c, round cells without processes
B, apex of the anterior horn
d, blood-vessels
e, sclerosis of white matter contiguous to
f, dense sclerosis of the margin of the anterior horn

process to a primary degeneration, it does not follow that this is the invariable rule. Both in the brain and in the cord inflammatory processes may be set up which after they have caused the destruction of a certain amount of nerve-substance come to an end by what we might call sclerotic cicatrization.

When a patch of inflammatory degeneration is formed and the acute changes have ceased, absorption of the detritus and exudation takes place exactly as in the case of ischæmic degeneration or softening. If the

destruction is extensive a permanent defect or hiatus will remain: if it is more limited after the disintegration and absorption of the nerve-elements there is left a tissue consisting of neuroglia (Fig. 271 *B*) and a network of vessels (*d*). This is partly old and persisting tissue, partly new-formed; its essential components are stellate or multipolar cells (*b*) whose processes freely anastomose. After absorption is complete a clear liquid containing a few leucocytes (*c*) lies in the meshes of the tissue. The result is a gray moist gelatinous patch, an example of what is called **gray gelatinous degeneration.**

Such gelatinous patches are usually surrounded by a zone in which the network of neurogliar fibres is much denser (*ef*), and might almost be called a feltwork, and the nerve-elements of the contiguous tissue are as it were embedded in the dense overgrowth which surrounds them (*e*). This change which in gelatinous patches is only marginal becomes in other cases general. Dense hyperplasia of the neuroglia may take place throughout the whole extent of a degenerating patch, and give rise to what is called hard sclerosis, or simply sclerosis (taken in a restricted sense).

Sclerotic patches such as we have described occur chiefly as the result of isolated local inflammations in the cord (Art. 659). Whether the disease known as multiple sclerosis is frequently or indeed at all a result of multiple inflammations is a question still unsettled. The occurrence of a disseminated miliary encephalitis and myelitis is in favor of an affirmative answer.

Although we are thus able in many cases to refer the causation of multiple sclerosis to primary degenerative or inflammatory processes, other cases are met with in which there are no grounds for such an assumption. These are cases both of ordinary multiple sclerosis and of the form which is described as **granular ependymal sclerosis.** The latter is a morbid change of the lining membrane of the cerebral ventricles characterized by the formation of small prominent gray granulations on its surface. In extreme cases these beset the ependyma so closely that it feels rough to the touch. Sometimes the little prominences coalesce and form reticulate or arabesque patterns on the surface.

Histologically the change consists in a new-formation of neuroglia, the fibrous feltwork being exceptionally dense in proportion to the number of cells or nuclei present. The cylindrical epithelium which invests the ventricle sometimes continues to cover the prominences, sometimes falls away and leaves them bare.

Diffuse forms of ependymal and subependymal sclerosis are also met with. If the process extends from the floor of the fourth ventricle to the deeper structures it may cause the destruction of the ganglion-cells in the gray nuclei of the cranial nerves.

We do not yet know the nature of the exciting cause of these affections: the fact that they are frequently associated with chronic meningitis

would suggest that they are of a chronic inflammatory character. In some cases circumvascular collections of cells are found in the subependymal tissue, and in this respect the granulations recall the structure of inflammatory papillomata of the skin (Art. 394).

Not infrequently extensive proliferations take place in the connective tissue about the central canal of the cord; they occur both in patches and as continuous longitudinal growths (Art. 637). As they are met with chiefly in connection with malformations of the canal, or in regions which experience shows to be liable to congenital anomaly, *i. e.* about the posterior columns, it seems fair to suppose that they depend on some congenital anomaly of structure in the tissues. Moreover, these proliferations are sometimes accompanied by sclerotic patches in other parts of the central nervous system, and hence it is not improbable that other multiple scleroses may occasionally be referable to disorders of development.

Many writers speak of all gray degenerations, hard or gelatinous, as scleroses. The etymology of the term (σκληρός hard and dry) would limit its application to the former variety. If however we extend the word to cover both varieties, and indeed they are genetically equivalent, we should perhaps speak of them as hard sclerosis and gelatinous sclerosis respectively.

The genesis of multiple sclerosis (called variously disseminated, insular, focal or cerebrospinal sclerosis) is still very differently explained by different writers. Some regard the degeneration of the nerve-elements as the primary lesion, others the hyperplasia of the neuroglia: others again describe the process as a chronic inflammation, or affirm that the overgrowth of fibrous tissue starts from the vessel-walls. In the author's own investigations, undertaken specially to determine these questions, he found that in recent cases the degenerative changes were so marked as to admit of no other supposition than that they were primary, and the multiplication of neuroglia-cells secondary. Cases do occur however where no patches of sclerosis can be found in which this pre-eminence of the degenerative changes is clearly apparent: and it is therefore not easy to disprove the statements of CHARCOT and others who regard the overgrowth of fibrous tissue as the primary cause (by compression) of the degeneration of the nerve-elements. Various facts go to show that forms of cerebrospinal sclerosis occur which are the result of anomalies or disorders of development, and are thus related to the periependymal growths met with in syringomyelia. It is also possible that other forms are due to the formation of multiple foci of inflammation.

References on multiple sclerosis:—LEYDEN, *Deutsche Klinik* XV. 1863 and *Klinik d. Rückenmarkskr.*; RINDFLEISCH, *Virch. Arch.* vol. 26; ZENKER, *Zeitschr. f. rat. Med.* XXIV. (1865), *D. Arch. f. klin. Med.* VIII. (1870); CHARCOT, *Diseases of the nervous system* I. London 1878; BOURNEVILLE, *La sclérose en plaques disséminées* Paris 1869; SCHÜLE, *D. Arch. f. klin. Med.* VIII.; BUCHWALD, *ibid.* X.; OTTO, *ibid.* X.; JOLLY, *Arch. f. Psych.* III.; ARNDT, *Virch. Arch.* vols. 61, 62; MOXON, *Guy's Hosp. Reports* XX. (1875); DICKINSON, CHEADLE, DREISCHFELD, *Med. Times and Gaz.* I. 1878; LEYDEN, *Charité-Annalen* III., *Arch. f. Psych.* VI. (sclerosis of bulbar nuclei), *Berl. klin. Woch.* 1878; SCHULTZE and RUMPF, *Cent. f. med. Wiss.* 1878; ERB, *Ziemssen's Cyclopædia* XIII.; FROMMANN, *Virch. Arch.* vol. 54, *Normale und path. Anat. d. Nervensystems* Jena 1876, *Die Gewebsveränd. bei*

mult. Sclerose Jena 1879; RIBBERT, *Virch. Arch.* vol. 90; FRIEDMANN, *Jahrb. f. Psych.* IV. (1883); BRAMWELL, *Diseases of the spinal cord* Edinburgh 1884 (for good figures); GOWERS, *Lancet* 1, 1886 (miliary sclerosis of brain).

On ependymal sclerosis and spinal periependymal sclerosis:—ROKITANSKY, *Handb. d. path. Anat.* I. (trans. Syd. Soc. London 1850); VIRCHOW, *Gesamm. Abhandlungen* Frankfort 1856; WEISS, *Œsterreich. med. Jahrb.* 1878; MAGNAN and MIERZEJEWSKY, *Arch. de physiol.* 1873; LEYDEN, *Klinik d. Rückenmarkskr.* II.; SCHULTZE, *Virch. Arch.* vols. 70, 87; FRIEDREICH, *ibid.* vol. 26; KAHLER and PICK, *Arch. f. Psych.* VIII.; EICKHOLT, *ibid.* X.; WESTPHAL, *Brain* VI. (1883); *Arch. f. Psych.* XVI. (1885); see also Art. 637.

On multiple and diffuse sclerosis in infants and children:—VON RECKLINGHAUSEN, *Verh. d. geburtshilfl. Gesellsch. zu Berlin* 1863; NEUREUTTER and STEINER, *Prager Vierteljahrsschr. f. pract. Heilk.* XX. (2); HUMPHREYS, *Med. Times and Gaz.* 2, 1877; POLLARD, *Lancet* 2, 1878; HARTDEGEN, *Arch. f. Psych.* XI.; POLLACK, *ibid.* XII.

651. When from simple or degenerative atrophy or inflammatory disturbance of nutrition the nerve-elements belonging to a considerable extent of tissue have perished, a diffuse hyperplasia of the connective tissue often sets in, and in advanced cases gives rise to a continuous in-

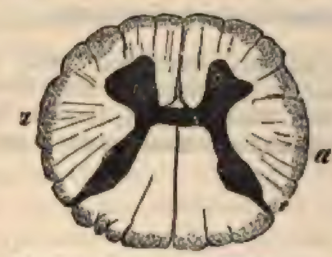

FIG. 272. MARGINAL SCLEROSIS OF THE CERVICAL CORD.

(*Diagrammatic:* × 3.)

a, sclerotic marginal zone

duration, or **diffuse sclerosis** as it is called. This change occurs for instance in simple atrophy of the cerebellar cortex (Art. 640). It is also common in atrophy of the marginal portions of the cord and in atrophy of the cerebral cortex, such as follows grave local disorder of nutrition from chronic inflammation of the pia mater. In the cord we may have a marginal sclerosis of this kind (Fig. 272), exactly resembling in its structure the scleroses we have already described. In the cortex of the cerebrum the induration is seldom great, and it is only on microscopical examination that the stellate neuroglia-cells and their fibrous processes are seen to be more abundant and more obvious than in the normal tissue (Art. 656, Fig. 273). Only when the antecedent atrophy has been very extensive is the hardening of the surface so palpable as to be recognizable by the finger.

This induration is secondary, but there is also a form of primary hyperplasia of the neuroglia which sometimes extends over considerable

portions of the central nervous system. In the general enlargement of the brain known as cerebral hypertrophy (Art. 633) the connective tissue is said to undergo a notable increase, giving the tissue a leathery or rubber-like consistency. This increase is more obvious in some peculiar indurative condition of particular portions of the brain, in which the normal form and aspect remain unchanged while the size is more or less enlarged. A convolution, a lobe, the corpus callosum, or the basal ganglia may thus become indurated *en masse;* or in the white matter ill-defined portions of tissue may be palpably harder than the parts around without any discoloration or other apparent change. Such indurations are all due to increase of the connective tissue: in some of them the brain-substance is transformed into a felted mass of delicate fibres containing a few scattered nerve-cells and nerve-fibres or in some parts none at all.

Diffuse scleroses cannot be sharply distinguished from the new-growths known as gliomata (Art. 662), and must be considered with them. We know nothing as to the causes of the change, though it is at least possible that they are dependent on some disturbance of the histological development of the tissues in which they occur.

References on diffuse sclerosis:—STRÜMPELL, *Arch. f. Psych.* IX; SIEMENS, *ibid.* X.; F. SCHULTZE, *ibid.* XI.; ZACHER, *ibid.* XIII.; GREIFF, *ibid.* XIV.; ERLER, *Diffuse Hirnsclerose* In. Diss. Tübingen 1881; COTARD, *Hémiatrophie cérébrale* Thèse de Paris 1868; JENDRÁSSIK and MARIE, *Arch. d. physiol.* V. 1885.

CHAPTER XCV.

INFLAMMATORY DISORDERS.

Serous inflammations.

652. Acute inflammatory exudations having a serous character take place into the substance of the brain and cord, into the membranous envelopes, and into the ventricles; and they give rise to grave and even fatal disturbance of the nervous functions.

Acute serous leptomeningitis is an affection in which a sudden congestive hyperæmia is followed by serous effusion into the subarachnoid and pia mater, and into the cerebral ventricles. The quantity of liquid found in the membranes at the time of death varies somewhat in different cases, but it is seldom great. The amount of blood in the congested vessels is also by no means constant. The ventricles are more or less dilated by the effusion (inflammatory internal hydrocephalus); sometimes so greatly that the convolutions are visibly depressed and flattened by pressure against the skull, while the cerebrospinal liquid is to some extent forced out of the subarachnoid spaces. The choroid plexuses are usually hyperæmic: the liquid in the ventricles and subarachnoid spaces is clear or slightly opalescent, and often contains minute flakes of fibrin. It is richer in albumen than the normal cerebrospinal liquid (HUGUENIN) and has floating in it a few pus-corpuscles. A few extravasated leucocytes may be seen in the neighborhood of some of the cortical vessels.

The disorder is commonest in infancy or early childhood, rare in adult life: it not infrequently accompanies the early stages of infective diseases such as measles or scarlatina. Very probably the œdema of the brain and meninges which sometimes supervenes in nephritis is in part at least of inflammatory origin. Perhaps too some of the cases in children are induced by the virus of epidemic cerebrospinal meningitis (Art. 653): frequently however no cause can be certainly assigned, though scrofula, rickets, and syphilis are believed to be predisposing conditions.

If the inflammatory œdema is not fatal it often disappears speedily, though sometimes it issues in a chronic inflammatory condition manifested by thickening of the meninges and permanent and increasing dilatation of the ventricles: this condition is called **chronic hydrocephalus,** and it sometimes comes on gradually and insidiously, that is to say without any markedly acute onset.

Of more common occurrence than these genuine diffuse serous exudations is the **localized inflammatory œdema** of the brain, cord, or membranes which is set up around foci of purulent, granulating, septic, tuberculous, syphilitic, or traumatic inflammation, or around new growths.

When the nervous tissue is the chief seat of œdema it looks moist and glistening, and is softer than in health. There is usually some accompanying circumvascular extravasation of leucocytes, partly in the adventitial sheaths of the vessels, partly in the surrounding tissue.

Purulent inflammations.

653. **Purulent leptomeningitis.** Purulent inflammation of the soft membranes (pia mater and subarachnoid tissue) is preceded first by the hyperæmia which is the first stage of all acute inflammations, then by serous exudation, and lastly by an extremely abundant accumulation of leucocytes in the circumvascular spaces. The veins, engorged and dilated, show streaks and patches of yellow along their course, and these rapidly extend, owing to the continued extravasation and infiltration. The opacity thus occasioned sometimes becomes so dense that the gyri of the brain and the surface of the cord are entirely concealed by it.

In simply purulent meningitis the exudation is composed of pus-corpuscles and extravasated liquid. In the sero-purulent and fibrino-purulent forms the exudation has a turbid muddy appearance, is more liquid, and contains granules, fibres, and (less frequently) hyaline clots of fibrin.

The exudation lies mainly in the clefts and spaces of the pia mater and subarachnoid tissue. The cells covering the trabeculæ of the connective tissue are for the most part cast off and degenerate. The veins and venules are thickly surrounded with leucocytes, and their walls penetrated by them. Sometimes the venous channel is crammed with leucocytes, especially towards its periphery; sometimes it is plugged with hyaline or granular coagula. When the arteries are surrounded by extravasated cells the adventitial coat is seen to be infiltrated with them, and the like is often true of the middle and inner coats.

The cortex of the brain and the cord are sometimes all but unaffected by the meningitis, being perhaps only slightly moister than usual, though it is frequently possible to demonstrate that changes have here and there taken place in the nerve-elements. In the cord we find swelling and partial disintegration of the axis-cylinders and degeneration in the medullary sheaths and nerve-roots. In the cortex the ganglion-cells become swollen and lose their finer processes.

Often enough the inflammatory change advances along the vessels to the cortex, the pial sheaths especially of the veins becoming filled with leucocytes. Or the change may extend to the nervous tissues in a

more generally diffused manner (Art. 654). The nerves issuing from the brain and cord are frequently infiltrated with cells.

When the inflammation extends through the transverse fissures of the base of the brain to the telæ choroideæ within the ventricles, a purulent or sero-purulent exudation is poured out, the liquid contents of the ventricles are augmented and rendered turbid, and the plexuses swell up and become covered over with pus or fibrino-purulent flakes. The ependyma and underlying brain-substance become moist and sometimes morbidly soft. When the distention of the ventricles is great the brain-substance is compressed, the gyri flattened, and the subarachnoid liquid forced out; the result being that the meningeal structures of the convexity become morbidly dry.

The seat and the extent of the inflammation vary greatly, depending of course on the exciting cause and on the manner in which it reaches the membranes. As to the nature and properties of the exciting causes we know little, but it is probable that micro-organisms are frequently at work, and probably also specifically distinct micro-organisms in different forms of the disease. In many cases micrococci have been found in the inflamed tissues, but it is not likely that they are always of the same kind or the same virulence.

Irritant matters (organic or not) may reach the meninges in the first place by way of the blood-vessels, in which case we might call the meningitis **embolic.**

If it chiefly attacks the convex surface it is described according to its distribution as local or general, unilateral or bilateral, meningitis of the convexity. Affecting the base it is called basal or basilar meningitis, and in the case of the cord spinal meningitis. In basal meningitis the cerebral axis is usually covered with pus, and the subarachnoid cisterns are much distended with the exudation.

Hæmatogenous purulent meningitis occurs in connection with traumatic pyæmia, gangrenous and croupous pneumonia, ulcerative tuberculous phthisis, endocarditis, gangrenous bed-sores, acute rheumatism, purulent pleurisy (empyema), scarlatina, typhoid, inflammation of the umbilicus in infants, etc. It is moreover the essential symptom of the infective disease known as **epidemic cerebrospinal meningitis.** As its name indicates the exudation in this disease extends over cord and brain, though by no means uniformly. When the inflammation is at its height it is usually purulent or fibrino-purulent, seldom hæmorrhagic, though cases rarely occur in which some small hæmorrhages do not appear. If death ensues within the first few days the quantity of exudation poured out is very small: sometimes nothing but a circumvascular infiltration of cells can be made out. In more advanced stages the subarachnoid liquid has a turbid whey-like appearance.

Both brain and cord are always involved, the cellular infiltration spreading from the pia mater along the vessels or directly to the cortex

of the brain and the substance of the cord. In addition to this small patches of inflammation (sometimes hæmorrhagic) are invariably found in the interior of the cerebrum: STRÜMPELL says they are usually very numerous. The smallest form mere clusters of cells in the pial sheaths of the vessels, the larger ones are quite extensive cellular infiltrations, and are accompanied by softening of the infiltrated region. If the patient survives these patches may become abscesses. Epidemic cerebrospinal meningitis is thus accompanied by encephalitis and myelitis, and even after cessation of and recovery from the meningeal affection **cerebral abscess** may be left as a sequela.

A second group of purulent inflammations are due to **extension** from contiguous parts, either by continuity or by way of the blood-vessels or lymphatics. Thus ostitis of a vertebra or of the petrous bone extends directly to the meninges: suppuration of the nose, frontal sinuses, base of the skull, scalp (ulcers, erysipelas, eczema), internal ear, and eye (panophthalmitis) lead to suppuration of the membranes, the various vessels which pass from the bone inwards to the membranes serving as channels of infection. Especially dangerous is puriform softening of thrombi within the veins of the skull or the sinuses of the dura mater. Lastly, purulent inflammation of the brain itself may lead to the like in the meninges. According to some (FISCHER, BILLROTH, HUGUENIN) simple concussion of the brain without any wound of the soft parts or bones occasionally gives rise to purulent meningitis; HUGUENIN and others say the same may occur after sun-stroke.

The inflammation in all these cases will naturally begin where the irritant or exciting cause first acts, that is to say, it begins as a local affection. The wide communication between the several subarachnoid spaces contributes however to the speedy extension and generalization of the process.

Purulent meningitis, especially when it is cerebral, is usually fatal, though in some cases of the epidemic cerebrospinal disease recovery takes place. In the latter event the exudation is in the course of time re-absorbed, but usually certain whitish thickenings of the membranes due to fibrous hyperplasia, and some permanent dilatation of the ventricles, remain as evidence of the attack. Under certain conditions not fully understood the acute inflammation passes into a chronic one, the membranes undergoing cellular infiltration and becoming remarkably thickened. When the inflammation has been mainly confined to the pia mater, it may result in atrophy of the underlying nervous tissues (Art. 656).

STRÜMPELL and WEIGERT have suggested that in cerebrospinal meningitis the infective virus may perhaps pass from the nose into the interior of the skull. The author is unable to accept the suggestion. Though he is convinced that purulent meningitis does not start from the nose, the phenomena of the epidemic affection appear to exclude that channel of infection. The manner in which the inflam-

matory change is distributed over the various parts of the meninges, the occurrence of numerous foci within the brain and cord, the frequent accompaniment of arthritis in various joints, etc., all indicate that the poison is spread by the channel of the blood-vessels, and thus reaches the central nervous system. The inflammation of the superior nasal meatus is a mere concomitant of the meningitis.

References on cerebrospinal meningitis:—ZIEMSSEN, *Ziemssen's Cylopædia* II.; WUNDERLICH, *Arch. d. Heilk.* V., VII.; ZENKER, *D. Arch. f. klin. Med.* I.; STRÜMPELL, *ibid.* XXX.; LANCEREAUX, *Traité d'anat. pathol.* II.; RADCLIFFE, *Reynolds' Syst. of med.* II. 1868; BURDON-SANDERSON, *Rep. of Med. Off. of Privy Council* 1866.

654. **Purulent encephalitis and myelitis.** In purulent meningitis the underlying nerve-tissue undergoes more or less extensive inflammatory change, and we might therefore very well describe the process as a meningoencephalitis or meningomyelitis. Under certain conditions however the inflammation of the brain or cord becomes the more marked feature, and this affects even the naked-eye appearance of the affected parts. This is especially the case in traumatic inflammations, set up by cuts, blows, stabs, or gun-shot wounds. The tearing and bruising of the tissue by the mechanical violence gives rise to disintegration or necrosis of the nerve elements, while the weapon which causes the injury may penetrate the substance of the brain or cord, or drive before it splinters of bone, or lacerate the blood-vessels and lead to hæmorrhage into the meninges or into the nerve-substance. If the wound becomes septic decomposition of the extravasated blood and of the damaged tissue takes place, and this induces violent purulent or putrid meningitis, encephalitis, or myelitis. The decomposing matters assume a dirty-brown, gray, or greenish color and give off a putrid odor. The actual inflammation begins with swelling of the nerve-substance and the formation of numerous points of hæmorrhage. The change first appears in the part near the injury, but often spreads widely, the hæmorrhagic extravasation extending deeply into the tissue, and also over a considerable area of the cortex beneath the inflamed pia mater. When the vessels are lacerated *ab initio* the swollen nerve-substance is tinged more or less deeply with yellow from the diffusion of the coloring-matter of the extravasated blood.

The hæmorrhagic foci lie always in the immediate neighborhood of small vessels, but as they grow larger they spread beyond the region of the adventitial lymph-sheaths into the nerve-tissue, and when the change is no longer quite recent they appear infiltrated with leucocytes which have left the vessels. This migration of leucocytes is the first stage of the suppurative process, and it steadily increases, until at length the nerve-tissue is as it were inundated by the multitude of extravasated cells, and presently undergoes degeneration and dissolution. When a portion of the tissue is thus liquefied and converted into a yellowish or

grayish or putrid pus-like cream, the encephalitis or myelitis has issued in **abscess.**

In like manner purulent meningeal inflammations due to other causes (*e. g.* suppuration of bone, or septic embolism) sometimes extend to the substance of the brain or cord and lead to abscess. As a rule however the process is not so violent or so rapid.

When irritant matters reach the interior of the brain or cord through the blood-vessels without affecting the meninges on the way, a local inflammation is set up which at first may not extend to the pia mater. If the irritant is one which has the power of setting up suppuration (such as the pyæmic micrococci), and lodges in a capillary or small vein, its first effect is to produce minute hæmorrhagic extravasations. These in the course of a few days become yellowish-white, with perhaps some slight blood-staining in the larger patches, and rapidly assume the appearance of abscesses. The number of extravasated white cells increases steadily, and at length the nerve-tissue breaks down and liquefies.

If at the same time one or more of the arteries have been blocked by embolism the inflammatory changes are accompanied or preceded by those characteristic of anæmic or hæmorrhagic necrosis (Art. 642). The final result is however the same: an abscess is formed, distinguished only from those already described by its possibly larger size.

Both forms of embolic suppuration occur under the same conditions as lead to purulent meningitis, namely pyæmia, endocarditis, suppuration or gangrene of the lung, putrid bronchitis, croupous pneumonia, cerebrospinal meningitis, etc.

Embolic abscesses arise most commonly in the cerebral hemispheres and cerebellum, rarely in the cerebral axis, and more rarely still in the cord: they are sometimes multiple. They contain as a rule creamy-yellow or pale-greenish pus. The smallest are as large as a pin's head, the larger ones may occupy the greater part of a lobe: most frequently they are from the size of a walnut to that of a hen's egg.

When recent the wall of an abscess has a broken-down appearance, the tissue around being œdematous and often beset with small points of hæmorrhage. If close beneath the pia mater an abscess generally sets up meningitis, and if it breaks into a ventricle a violent inflammation of that region ensues.

Only the very smallest abscesses are capable of absorption and repair by cicatrization. The larger ones, if not fatal by pressure or meningitis, become enclosed in a granulating capsule or membrane and may exist for years in a quiescent state. So early as four weeks after its first appearance an abscess may be walled off from the surrounding tissue by a gray or grayish-red zone: in the course of months the zone grows broader and firmer, measuring from 2 to 5 mm. across. This is simply granulation tissue, which by and by is transformed into cicatricial fibrous tissue. In old abscesses the enclosing membrane is thus

made up of an inner granulating layer of cells and vessels and an outer fibrous layer.

Once encapsuled or 'encysted' in this way, the abscess slowly grows by the accumulation of pus derived from the granulating membrane; this secretion is probably not continuous, and in long-standing abscesses must be very slight. The surrounding brain-tissue is compressed, and sometimes atrophies or even degenerates and breaks down. At any moment moreover inflammatory œdema and fresh cellular infiltration may be set up in the compressed tissue, and these give rise to disturbance of the cerebral functions and often enough lead to a fatal issue. Nor is the danger of perforation into a ventricle or extension to the pia mater by any means removed when the abscess is encapsuled. Cerebellar abscesses may by pressure on the veins of Galen set up dropsy of the ventricles. Recovery from a large abscess is indeed possible only after surgical evacuation of its contents.

References on cerebral abscess:—LEBERT, *Virch. Arch.* vol. 10; SCHOTT, *Würzburg. med. Zeitschr.* II. (1862); BILLROTH, *Arch. d. Heilk.* 1862; HUGUENIN, *Ziemssen's Cyclopædia* XII.; R. MEYER, *Zur Path. d. Hirnabscesse* In. Diss. Zürich, 1867; MAAS, *Berl. klin. Woch.* 1869; WYSS, *Jahrb. d. Kinderheilk.* IV. (1871); CRUVEILHIER, *Anat. pathologique* part 33; NAUWERCK, *D. Arch. f. klin. med.* XXIX; RETTELHEIM, *ibid.* XXXV. 1835 (abscess after empyema); EISELSBERG, *ibid.* (abscess after sunstroke); TOYNBEE, *Diseases of the ear* London 1868; GULL, *Guy's Hosp. Reports* III. (1857), *Reynolds' Syst. of med.* II. London 1868; HAYEM, *Arch. de physiol.* 1868.

Chronic Meningitis.

655. **Secondary forms of chronic leptomeningitis.** Chronic inflammation of the cranial or vertebral bones, or of the dura mater, are apt sooner or later to extend to the arachnoid, the subarachnoid tissue, and the pia mater. This extension occurs most commonly in tuberculous and syphilitic disease, though it is also met with in other inflammations, such as for instance are set up by mechanical injury to the bones. The idiopathic inflammation known as internal pachymeningitis, which is characterized by the formation of false-membranes and adhesions on the inner surface of the dura mater, sometimes extends to the inner meninges also.

The arachnoid having no vessels of its own is only passively affected by the inflammatory process, and undergoes more or less extensive degenerative changes. In the pia mater on the other hand, and in the vascular portions of the subarachnoid meshwork, inflammatory disturbances of the circulation make their appearance, and lead in the first place to infiltration of the latter tissue and of the arachnoid.

The next stage varies with the character of the inflammation. If it be of tuberculous or syphilitic origin, in course of time the arachnoid, the subarachnoid tissue, and the pia mater become milky and thickened,

partly from cellular infiltration, partly from the new-formation of fibrous tissue. Adhesions are not infrequently formed between the dura mater and the arachnoid. These are usually most dense and abundant in traumatic pachymeningitis; in the idiopathic form they are soft, fibrinous, and vascular.

But secondary chronic inflammations of the inner meninges are still more frequently the result of acute or chronic disease of the brain and cord. Every subpial inflammatory and degenerative process affecting the nerve-substance is capable of inducing meningeal inflammation: and tumors of the brain or cord act in like manner either directly, or through destructive changes in their own substance or in the tissue about them.

The pia mater and the surface of the central nervous organs stand in the closest possible connection, and in all degenerative processes affecting the latter, whether they are inflammatory or not, some of the products of disintegration are apt to reach the pial tissue and the subarachnoid spaces, and there give rise to turbidity or (in the case of hæmorrhage) yellow or brown pigmentation. The turbidity is more marked when the disintegrated matters possess irritating properties and excite inflammation. Then abundant extravasation of leucocytes ensues, and in time a more or less extensive fibrous hyperplasia is the result. In many cases the hyperplasia is well marked (Art. 642, Fig. 260), the meninges becoming dense, thick, white, and opaque. Both the subarachnoid and the arachnoid tissue take part with the pia mater in this hyperplasia, the trabeculæ of the former becoming thicker and coarser, new trabeculæ being formed, and the characteristic structure of the tissues obscured or altered. Calcareous concretions are common in the thickened membranes; and peculiar-looking cells are aggregated into spherical clusters, then become homogeneous, and lastly calcified, and are surrounded by tiny capsules of cells and new-formed fibrous tissue.

Secondary meningitis of the spinal cord is similar to that of the brain, and follows upon inflammations of the vertebræ or spinal dura mater. In some cases the inflammation also extends to the substance of the cord itself.

656. **Hæmatogenous chronic leptomeningitis.** We have already pointed out (Arts. 652, 653) that acute meningitis of hæmatogenous origin, if not fatal, may issue in recovery by re-absorption of the exudation; but this is frequently accompanied by some thickening of the membranes due to new-formation of fibrous tissue. In certain not fully understood conditions the acute disorder passes into a chronic form, characterized by persistent cellular infiltration, and consequent thickening and opacity of the meninges; chronic internal hydrocephalus is a further sequela.

But there are other forms of chronic leptomeningitis which as to their causation, rise, and progress, differ notably from the foregoing.

We refer to those chronic (more rarely acute or subacute) inflammatory processes which are the most frequent though not invariable antecedent of certain mental disorders, especially that known as paralytic dementia or **progressive paralysis of the insane.** The processes in question and the mental disease as commonly defined are not exactly co-extensive: on the one hand they may be absent in cases where the mental disease exists, and on the other they are met with in cases where the symptoms if any have been other than mental.

The morbid conditions referred to have certainly not the same ætiological or clinical significance in all cases: they may be divided into two groups according to their anatomical characters, in other words according to their situation and the nature of the textural changes they induce.

In the first place we have changes affecting mainly the arachnoid and subarachnoid tissues and giving them a white opaque appearance, the opacity being limited to spots and streaks or more uniformly diffused: it is most apparent over the sulci and the subarachnoid cisterns, and occurs both at the base and on the convexity of the brain. It is still doubtful whether these opacities are always of inflammatory origin. They are histologically due to fibrous thickening, endothelial hyperplasia, or more rarely to cellular infiltration. If we are to reckon them provisionally as due to chronic inflammation, this would probably be best described as **chronic arachnitis** or **external leptomeningitis.** As to their causation they are observed in connection with chronic venous engorgement and with certain morbid states of the blood, as in alcoholism and chronic nephritis.

Of greater importance than the changes just mentioned, which after all can hardly be supposed to induce grave disorder of the nervous functions, are certain chronic affections which involve chiefly the pia mater and underlying nerve-tissue: in their later stages at least they are unmistakably inflammatory, and are therefore appropriately included under the terms **chronic meningoencephalitis** and **meningomyelitis.**

When the morbid process is well advanced the soft membranes, especially the pia mater, are visibly milky and opaque, the change showing best in the sulci along the blood-vessels, and sometimes also on the ridges of the convolutions. It is most common in the anterior parts of the brain, namely the frontal and parietal lobes, the other parts being little or not at all affected. Cases however are described in which the change is most marked in the temporal lobes.

The most striking of the textural changes is undoubtedly the cellular infiltration which pervades the pia mater (Fig. 273 *h*), and to a less degree the subarachnoid tissue (*b*). This is occasionally accompanied by a more or less extensive fibrous hyperplasia of these structures. In later stages accumulations of leucocytes (i_1), and in smaller quantity red blood-cells and brown or yellow pigment (i_2), appear in the adventi-

tial sheaths of the cortical vessels, and sometimes even of those supplying the white matter. But no great accumulations of cells are as a rule met with in the mass of the brain-substance itself. The cellular infiltration is not uniform, varying much even within the tissue of the pia mater. In the cortex comparatively few vessels are surrounded by masses of cells, and in the white matter perhaps one or two at most. Some of the vessels however show hyaline or fibrous thickening of the adventitial coat.

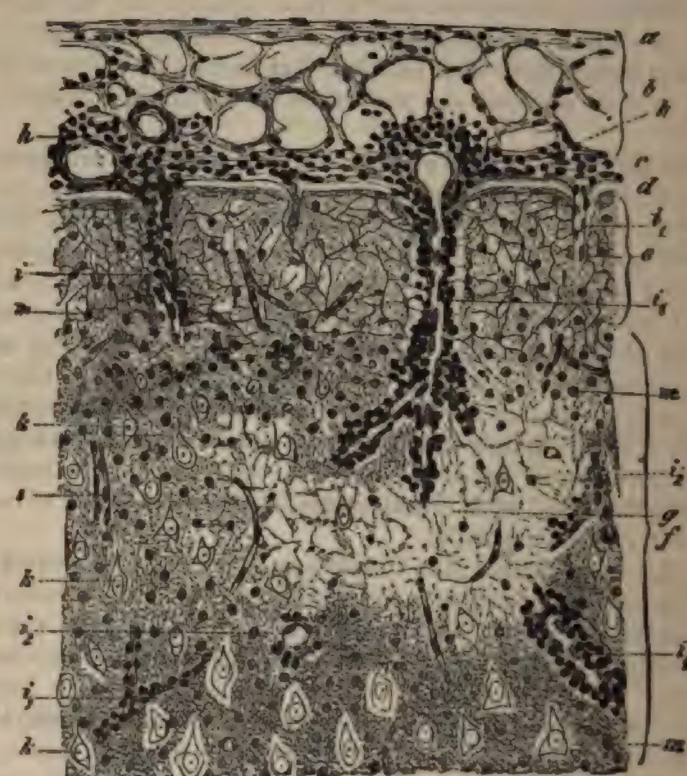

FIG. 273. CHRONIC MENINGOENCEPHALITIS WITH ATROPHY OF THE CORTEX.

(Section hardened with Müller's fluid and alcohol, stained with alum-carmine and ammonia carminate, and mounted in Canada Balsam: × 150.)

a, arachnoid
b, subarachnoid tissue
c, pia mater
d, superficial layer of cortex
e, layer of small pyramidal cells; the cells have disappared, and numerous stellate figures composed of glistening fibres have taken their place
f, layer of large pyramidal cells,
g, many of these have disappeared, a delicate reticulum remaining
h, cellular infiltration of pia mater
i, unaltered blood-vessel
i_1, pial sheath of vessel filled with leucocytes
i_2, pial sheath filled with blood-cells and pigment
k, ganglion-cell (of the third layer)
m, neuroglia-cells

The nerve-substance of the cortex is probably never entirely normal

in these cases; though it is not always easy to demonstrate the changes that exist. In very chronic cases it is often visibly atrophied, its depth being diminished to a half or a third of the normal: but the atrophy is far from being always uniform over the affected area, being sometimes most marked in particular convolutions or parts thereof. The atrophied areas are usually pale, seldom reddened, and are occasionally somewhat indurated.

As the white matter is at the same time diminished the affected portion of the brain is on the whole perceptibly smaller, and the space left vacant by the shrinking is filled up by liquid collecting in the subarachnoid tissue. Sometimes too the ventricles are dilated and their ependyma beset with granulations (Art. 650). When the atrophy is extreme the brain is sometimes so remarkably shrunken that it weighs less than 1000 grammes. The affection is therefore aptly described as **atrophic meningoencephalitis.**

The outer layers of the gray matter are usually the most altered. In both pyramidal-cell layers (*e f*) the number of cells is diminished, and here and there are patches in which all of them have disappeared (*g*). In sections mounted in Canada balsam the loss of the nerve-elements causes the tissue (normally so densely granular) to look as if it were full of holes and gaps, nothing but a fine scarcely-visible reticulum remaining at certain points. The layer (*e*) of small ganglion-cells (pyramidal cells) shows this in the most marked way: the neuroglia may be hardly apparent (*f*), or it shows as a meshwork of glistening fibres (*e*) interlacing irregularly or disposed in stellate patterns. The points of intersection of the fibres are sometimes occupied by nuclei, and now and then it is possible to demonstrate that the fibres are simply processes of the neuroglia cells. When the cortex is not visibly thinned the atrophy is slight and hardly to be made out in Canada-balsam preparations. Perosmic acid brings out the fact that some of the nerve-cells are breaking down, with or without the formation of fat-granules.

The medullary or white matter of the brain is often in these cases not only shrunken but also interspersed with foci of degeneration.

The cord and pia mater is in like manner subject to cellular infiltration: not infrequently there is also present some degeneration and sclerosis of the pyramidal and of the posterior columns (Arts. 647, 648).

In the disease known as **paralytic dementia** or progressive paralysis, which is characterized by loss of intellectual power, emotional derangement, and illusions, the atrophic form of hæmatogenous chronic meningoencephalitis is an extremely common lesion. It must however be mentioned that not only this form but other chronic inflammations from traumatic injury of the head may lead to progressive paralysis, and that in patients who have died of the latter disease all that is found in some cases is simple non-inflammatory degeneration of the cortex and meninges. It would thus appear that the disordered nutrition and degeneration of the ganglion-cells and nerve-fibres is the essential feature; the

inflammatory infiltration and the increase of the fibrous structures serve to indicate the nature of the process (Art. 657) but do not determine the clinical symptoms.

Bayle describes progressive paralysis as a chronic arachnitis, Calmeil as chronic periencephalitis, Perchappe as softening of the brain, Tuczek as chronic meningitis, Magnan as diffuse interstitial meningoencephalitis, Mendel as diffuse interstitial cortical encephalitis, Luys as diffuse interstitial sclerosis. Most writers regard the affection as an inflammation corresponding in general to what we have described as chronic meningoencephalitis. The interpretations given to the various morbid appearances differ widely. Thus Mierzejewsky and Voisin regard the fibrils and stellate cells, which are often so markedly visible in the atrophied cortex, as fibrinous. Mendel, Lubimuff, Selvili, and others attribute much importance to the stellate cells, and think that they multiply considerably. This can only occur in a very few cases and to a limited extent. As a rule they are not increased in number, but they are merely more visible in the absence of the nerve-elements. The statements sometimes made as to multiplication of the ganglion-cells cannot be regarded as proven.

It is frequently asserted that in progressive paralysis the pia mater is abnormally adherent to the brain-surface, tearing away the latter as it is stripped off —but the test is of little value. It often fails where there is the most marked change both in pia mater and cortex, and only shows that the brain-substance is abnormally soft: the effect is in part at least due to post-mortem changes. It is better not to try at all to strip off the pia mater, for it renders the brain almost useless for minute examination afterwards.

Mierzejewsky and others have affirmed that in this affection filamentous processes and ramified connective-tissue cells are found attached to the vessels of the cortex when isolated: the description is accurate, but the phenomenon is not characteristic, as it is found in connection with other morbid conditions and even occasionally in healthy brains. Simon, Arndt, Schüle, and Greiff have found in paralytic and other brains patches of clear hyaline substance in the neighborhood of the vessels.

According to Tuczek (*Neurol. Centralb.* 1883) in paralytic dementia the medullated nerve-fibres of the cortex are especially apt to be lost, and that chiefly in the island of Reil and Broca's convolution (left inferior-frontal); while the ascending-frontal gyrus, the paracental lobule, the second-temporal gyrus, and the parietal and occipital lobes are usually free from change. The loss of fibres is first apparent in the superficial layers.

In one case of chronic basal meningitis Manz (*Graefe's Arch. f. Ophthalm.* 1883) met with large endothelial growths in the pial sheath of the optic nerve, the nerve itself being atrophied.

On the morbid changes in the brain in progressive paralysis (general paralysis of the insane):—Meynert, *Viertelj. f. Psych.* 1868; Westphal, *Arch. f. Psych.* I.; Simon, *ibid.* II.; Greiff, *ibid.* XIV.; Zacher, *ibid.* XIII., XIV.; Meschede, *Virch. Arch.* vols. 34, 56; Tigges, *Allg. Zeitschr. f. Psych.* XX.; Schüle, *ibid.* XXV.; Lubimuff, *Virch. Arch.* vol. 55, *Arch. f. Psych.* 1874; Mierzejewsky, *Études sur les lésions cérébrales dans la paralysie générale* Paris 1875, *Arch. de physiol.* 1876; Voisin, *Traité de la paral. gén. des aliénés* Paris 1879; Mendel, *Die progr. Paral. d. Irren* Berlin 1880, *Berl. klin. Woch.* 1882, *Neurol. Centralb.* 1883; Schultze, *Arch. f. Psych.* XI.; Selvili, *Zur path. Anat. d. Dementia paral.* In. Diss. Zürich 1876; Luys, *Gaz. méd.* 33, 1876; Klebs, *Prag. med. Woch.* 1879; Emminghaus, *Allg. Psychopathologie* Leipzig 1878; Tuczek, *Dementia paralytica* Berlin 1884; Kräpelin, *Arch. f. Psych.* XV. 1884; Hartmann, *ibid.* XVI. 1885 (mental disorder following injury to the head).

On like changes in the cord:—TÜRCK, *Wiener Sitzungsber.* LI., LII., LVI.; WESTPHAL, *Virch. Arch.* vols. 39, 40; MAGNAN, *Gaz. des hôpitaux* 14, 1876; STEWART, *Glasgow Med. Journ.* 1886.

657. The **ætiology** of hæmatogenous chronic meningoencephalitis is in many respects imperfectly understood. Hereditary predisposition, severe mental labor, exciting or exhausting influences of every kind, etc. have all been observed as antecedent conditions, and in such cases the hypothesis of an infective or toxic exciting cause seems to be excluded: such a cause is conceivable only in cases where the process is associated with diseases like cerebrospinal meningitis, typhoid, erysipelas, articular rheumatism, etc. And even here the secondary affection may well be the result of disordered nutrition rather than of any special extension of the primary disease.

Most cases of chronic meningoencephalitis and meningomyelitis would thus appear to be in their inception mainly dependent on degenerative changes due to excessive functional activity or to disorder of the circulation.

In recent cases of mental disorder presenting the same symptoms as the lesion we are considering, that is to say in what is clinically progressive paralysis, the changes found are frequently degenerative only, little if any evidence of inflammatory disease being discoverable. White turbidity of the pia mater is the chief of these changes, and it is due to an accumulation in the tissue of small globules and granules of fat, fatty and broken-down cells, and occasionally fat-granule cells. This detritus cannot have been wholly produced at the points where it is found by the degeneration merely of the meningeal endothelium or of extravasated cells; it must at least in part be derived from the brain-substance: and as a fact like matters are found in small quantity in the pial sheaths of the cortical vessels, while the vessel-walls themselves show here and there spots of fatty degeneration. It is also of special interest to note that some of the ganglion-cells are likewise fatty.

It often happens that no signs of inflammation appear at the sites of degeneration, though there are often small hæmorrhagic extravasations or pigmentary deposits to indicate that the circulation has been disturbed. It must be remembered that congestive hyperæmia alone, such as frequently accompanies excessive functional activity, is capable of increasing the intracranial pressure, and thus of compressing the capillaries, retarding the circulation, and bringing about local anæmia and engorgement with all their consequences.

But although simple disturbances of circulation and nutrition play an important part in the causation of progressive paralysis, it must not be forgotten that in other parts of the brain or cord, such as the centrum ovale or the columns of gray matter, close examination may reveal collections of leucocytes in the adventitial sheaths of the vessels. These

are sometimes very abundant, and can hardly be regarded as mere accumulations from stasis in the lymphatics, but are almost certainly evidence of inflammation. The occasional combination of multiple sclerosis (like that of recent encephalitis and myelitis) with meningo-encephalitis is of interest as showing that the process is one which in some instances at least is not limited to the cortex, but affects the whole central nervous system. As the disease becomes more advanced, the evidences of inflammation become more numerous, a result probably of the continuous action of the same exciting causes as first induced it.

These observations hold of a number of the cases: in others the inflammatory nature of the lesion is apparent from the commencement. Some acute cases are indeed described in which *post mortem* the hyperæmia and saturation of the brain with liquid effusion were unmistakable.

Chronic leptomeningitis is somewhat frequently associated with exudative pachymeningitis (Art. 664).

The apparent prominence of the neurogliar meshwork with its stellate cells in the atrophied portions of the cortex is at first due simply to the disappearance of the nerve-elements. Later on an actual multiplication and hyperplasia of the neuroglia-cells may take place, as in other atrophies of nerve-tissue.

The occasional combination of meningoencephalitis with degeneration and sclerosis of the posterior columns of the cord would indicate that the latter lesion is secondary, resembling in origin those changes we have already described. The spinal pia mater when it is affected at all is apt to be most thickened over the posterior half of the cord, and this has probably something to do with the locality of the sclerosis. The degeneration of the pyramidal tracts which is sometimes met with in the disease is perhaps dependent on the degeneration of the motor centres in the cortex (FLECHSIG), though this is questioned by WESTPHAL (Art. 647).

Chronic leptomeningitis of the cord alone, apart from the secondary forms dependent on inflammation of the dura mater, vertebræ, or cord-substance, is most commonly a termination of an acute attack. Most writers state that it may also be due to catching cold, and it sometimes follows mechanical injury. It is marked by the presence in the soft membranes of opacities, thickenings, and adhesions to the dura mater, and at times by increase and turbidity of the subarachnoid liquid. Marginal sclerosis, multiple sclerosis, and degenerations of some of the columns are occasionally present in the same case.

Cicatrization and Sclerosis.

658. **Repair of wounds of the brain and cord.** Bruises, cuts, stabs, and gun-shot wounds of the brain are usually fatal from the supervention of purulent meningitis and encephalitis. More rarely

abscesses are formed which are evacuated and healed up by granulation and cicatrization. It is only when the wound is aseptic or is at once protected from septic infection that we can expect healing without suppuration.

The destructive changes set up by a traumatic lesion vary with its nature. Bruises and contusions are the most dangerous, stabs and punctures the least so.

When the brain is punctured (Fig. 274 *a*), as by a dagger-wound, in the first place hæmorrhage takes place, and the tissue immediately contiguous is thereby destroyed. A patch of anæmic or hæmorrhagic necrotic softening (*b*) is thus produced, the meninges overlying the part being usually infiltrated with blood.

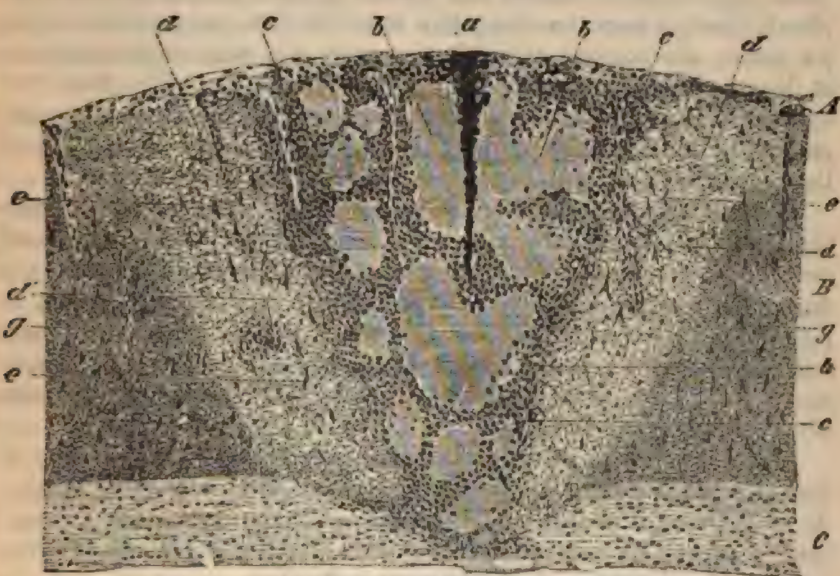

FIG. 274. ENCEPHALITIS EXPERIMENTALLY PRODUCED BY A PUNCTURE.

(From a rabbit's brain 12 days after the injury: section hardened in Müller's liquid, stained with hæmatoxylin and neutral carmine, and mounted in Canada balsam : × 25.)

A, meninges — *B*, cortex — *C*, white matter

a, puncture
b, necrotic tissue, granular and denucleated
c, zone of inflammatory cellular infiltration
d, zone of degeneration
e, swollen and degenerate ganglion-cells
g, normal cortical substance

At the boundary between living and dead tissue a more or less intense inflammation (*c*) sets in after a few hours, and this by degrees constitutes a zone of demarcation. The inflammatory process advances mainly along the vessels (*c*) entering from the pia mater, and in a few days the inflamed tissue softens and liquefies, while the inflammatory cellular infiltration extends more and more into the necrotic patch (*b*). The

latter also liquefies and is absorbed, though months or years may pass before all the detritus is carried off.

Around the inflamed region the nerve-substance suffers from impaired nutrition, and a considerable portion of it undergoes degeneration (*d*), indicated by swelling, fatty change, fragmentation and disintegration of the ganglion-cells (*e*) and nerve-fibres. The inflammatory zone is thus surrounded by a broad zone of degeneration.

During the first few weeks the inflammatory zone is chiefly made up of vessels, small round-cells, larger formative cells, and fat-granule and pigment-carrying cells. The latter are always very abundant so long as absorption of the products of disintegration and extravasation goes on, the fat-granule cells being visible also in the zone of degeneration. After some weeks or months new fibrous tissue is gradually elaborated, plainly starting from the vessels that enter the inflamed region from the pia mater: the necrotic region is thus more and more surrounded and at length filled up with new-formed fibrous tissue. The fibres are sometimes close-set and wavy, sometimes loose and areolar, and are the product of the fibroblasts derived from the extravasated leucocytes and the connective-tissue cells of the pia mater and the vessel-sheaths.

This **cicatrization** is a very slow process, and after months or years the scar may still contain multitudes of round-cells. The encapsuled necrotic patch only disappears after the lapse of many months, and the degenerative changes external to the inflamed region persist as long or longer. Rarely does the degeneration result in fibrous hyperplasia and sclerosis, though when this happens the sclerosis is apt to be very extensive. In like manner the fibrous thickening of the wounded pia mater often extends over a large area.

This is the process of repair in comparatively small wounds: it is of course modified if there has been extensive laceration of the brain-tissue. As we mentioned in Art. 645 in speaking of contusions, the development of fibrous tissue is apt to be slight and incomplete, and the process takes the form of progressive **ischæmic softening.**

This account of the repair of the wounds of the brain is based partly on observations made by the author on human injuries, partly on experiments made for him by KAMMERER upon rabbits. The process of healing can be readily followed in punctured wounds made under antiseptic precautions with recently heated needles. The oldest wound examined in a patient was 21 months old, and was due to a knife-stab penetrating the ascending-frontal convolution of a young man. The necrotic patch was not then fully absorbed, and the scar was still surrounded by a broad zone of degeneration, which like the scar contained numerous fat-granule and pigment-carrying cells.

References:—BRUNS, *Die chir. Krankheiten u. Verletz. d. Gehirnes u. s. Umhüllungen* Tübingen 1854; STROMEYER, *Verletz. u. chir. Krankh. d. Kopfes* Freiburg 1864; BERGMANN, *Deutsche Chirurgie* part 30; VIRCHOW, *Virch. Arch.* vol. 50; GLUGE, *Abhandl. z Physiol. u. Path.* Jena 1841 (experiments on encephalitis); HASSE and KÖLLIKER, *Zeitschr. f. rat. Med.* IV. (1846); JOLLY, *Stud. aus d.*

Inst. f. exp. Path. Vienna 1870; HAYEM, *Etudes sur les diverses formes d'encéphalite* Paris 1868; KLEBS, *Path. Anat. d. Schusswunden* Leipzig 1872; ZIEGLER, *Sitzungsber. d. phys.-med. Gesell. in Würzburg* 1878.

659. Both in the brain and cord we meet with localized or disseminated hæmatogenous inflammation, which like the localized degenerations lead partly to permanent loss of substance, partly to gray degeneration and sclerosis. **Encephalitis** is the name given to the affection of the brain, **myelitis** to that of the cord.

It is in the first place to be kept in mind (Art. 653) that in epidemic cerebrospinal meningitis patches of encephalitis and myelitis are of constant occurrence. In the meningitic processes associated with progressive paralysis inflammatory foci are found in the interior of the brain and cord, and sometimes in the pial sheaths of the nerve-roots. But these deeper inflammations also take place in the absence of meningitis, both in connection with infective disorders and idiopathically.

Thus in typhoid, variola, acute rheumatism, pyæmia, puerperal fevers, ulcerative phthisis, etc. multiple encephalitis is not rare, while in hydrophobia (so-called *lyssa*) patches of inflammation scattered through the whole central nervous system, but chiefly in the base of the brain and the cord, have been described by a number of writers (KOLESSNIKOW, FOREL, GOWERS, WELLER). They are very common in tuberculosis (Art. 660).

Frequently too these patches occur without any apparent exciting cause, and are then attributed vaguely to cold or some such injurious influence. According to certain authorities violent irritation of peripheral nerves is capable of setting up myelitis; though it is more likely that the spinal diseases thus induced are due to ischæmic or hæmorrhagic softening.

The smaller and more recent patches are not visible to the naked eye, being little more than circumvascular cellular infiltrations. When they are somewhat larger they are usually seen as red or pink spots, which are very distinct when in the white matter. Sometimes they contain little extravasations, and under certain conditions the whole patch resembles one of hæmorrhagic softening.

The smaller patches occasionally heal without leaving a trace. In the larger ones there is always some destruction of nerve-tissue, a small cyst (Art. 642), a gray gelatinous patch (Fig. 271, Art. 650), a sclerosis, or a scar remaining after the cessation of the inflammatory disturbance and the absorption of detritus and exudation.

In the brain recent **multiple encephalitis** is found in many acute mental disorders: sometimes the patches are extraordinarily numerous. As to the issue of this form of disease we know little, though it is possible that it terminates in multiple sclerosis. As to the larger myelitic foci and their consequences we are better informed.

In the first place the cord is subject to acute inflammation affecting

chiefly the gray matter, and described as central myelitis or poliomyelitis ($\pi o \lambda \iota o s$ gray). **Anterior poliomyelitis** is the commonest form (Figs. 275, 276), the inflammation being limited to one or both anterior horns. More rarely it extends to the posterior horns or to the entire section of the gray columns (Fig. 277).

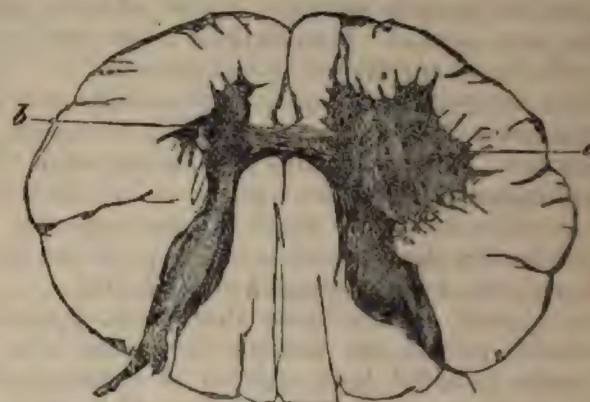

FIG. 275. SCLEROSIS AND SHRINKING OF THE LEFT ANTERIOR HORN.

(Section taken at the level of the fourth cervical nerve from a case of infantile paralysis (acute anterior poliomyelitis) in a child of 3½ : hardened in Müller's fluid, stained with neutral carmine, and mounted in Canada balsam : × 7.)

a, normal anterior horn with ganglion cells
b, atrophied and shrunken horn

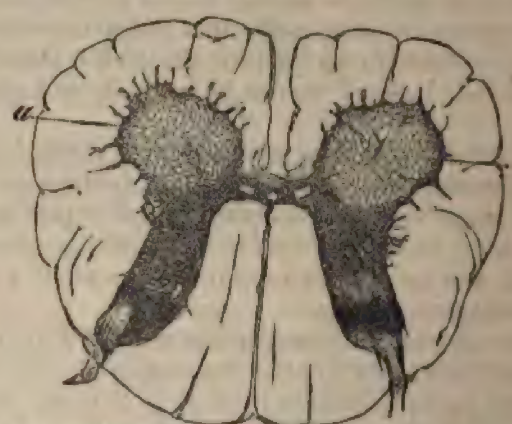

FIG. 276. GELATINOUS DEGENERATION OF BOTH ANTERIOR HORNS.

(Section taken from lumbar region : case of acute anterior poliomyelitis in a man of 40: preparation treated as in last figure : × 6.)

a, anterior horns

The disease chiefly attacks children less than four years old, and hence the clinical name of **infantile spinal paralysis**; it is rare in adults. Its onset is acute, there is usually fever, and soon paralysis, which is

the course of a week passes away to some extent. So far as our knowledge goes the inflammation is hæmorrhagic in character, and gives rise to functional disorder partly by destruction of tissue and partly by pressure. The preference shown for the anterior columns and especially for the inner two-thirds of each appears to be due to the fact that these parts constitute a special vascular territory distinct from the white matter. The length of the affected region varies from about 0.5 to 4 centimetres, though cases occur in which much larger segments of the cord are attacked.

The number of ganglion-cells and nerve-fibres destroyed depends on the severity of the inflammation: sometimes indeed the whole of the nerve-tissue perishes outright.

In the course of weeks or months the exudation and the products of disintegration are absorbed. If the neuroglia as well as the nerve-elements is destroyed a small cyst is formed. If the neuroglia persists and

FIG. 277. SCLEROSIS AND SHRINKING OF THE ENTIRE GRAY MATTER.
(Section taken from lower dorsal region of a man of 30 suffering from acute anterior poliomyelitis: preparation treated as in last figure: × 6.)
a, site of gray matter
b, sclerosis of posterior columns

undergoes a moderate hyperplasia, the substance of the anterior horn is transformed into a gray gelatinous mass (Figs. 271, 276), consisting of a loose reticulum containing liquid in its wide meshes. When the hyperplasia is considerable the tissue becomes close-textured, firm, and sclerotic (Fig. 275), consisting of a felted mass of fine fibrils with scattered nuclei. The vessel-walls are in general thickened, the adventitial lymph-spaces are dilated, and contain at least in the earlier stages round-cells and granular cells. When the nerve-elements are not entirely destroyed the sclerotic tissue still encloses a few ganglion-cells (Fig. 278 *b*) and nerve-fibres.

The anterior roots and the peripheral motor nerves become atrophied when the ganglion-cells are destroyed, and assume a gray wasted appearance. The muscles supplied by them likewise atrophy.

When the inflammation affects the gray matter over its whole cross-section, the horns become after a time strangely warped and distorted, and presently undergo gelatinous degeneration or sclerosis (Fig. 277).

The white columns are frequently affected by secondary extension of inflammation from the gray matter. Sometimes however the white matter is inflamed from the beginning, and we have **leukomyelitis** (λευκος white) associated with poliomyelitis. In such cases the whole cross-section of the cord or the greater part of it undergoes destructive inflammation (**transverse myelitis**), and afterwards gelatinous and sclerotic changes (Fig. 278). The disease moreover frequently extends over a considerable segment of the cord. Secondary ascending and descending degeneration of the tracts after a time follows on the local lesion.

Myelitic foci are usually single, though sometimes they are multiple, as in disseminated myelitis. The multiple patches are usually small, and may be scattered throughout the whole cord. When myelitis

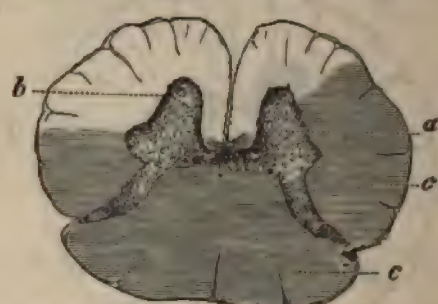

FIG. 278. SCLEROSIS AFTER ACUTE TRANSVERSE MYELITIS.

(Section taken from a man of 40 at the level of the lower dorsal region: hardened in Müller's fluid, stained with carmine, and mounted in Canada balsam: × 6.)

a, gelatinous change in gray matter
b, surviving ganglion-cells
c, atrophied and sclerotic white matter

attacks the region of the bulbar nuclei it gives rise to acute **glosso-labio-pharyngeal or bulbar paralysis.**

Under conditions analogous to those which lead to acute poliomyelitis in children we may apparently have an acute inflammation of the cortical gray matter or **acute polioencephalitis** (STRÜMPELL), the result of which is **infantile cerebral paralysis.** In its later stages it is characterized by loss of substance in the convolutions, resembling the congenital condition known as porencephalia (Art. 630).

BENEDIKT (*Virch. Arch.* vol. 64), KOLESSNIKOW (*ibid.* vol. 85), FOREL (*Zeitschr. f. Thiermed.* III.), ALLBUTT (*Trans. Path. Soc.* XXIII. 1872), GOWERS (*ibid.* XXVIII. 1878), ROSS (*ibid.* XXX. 1880), COATS, *Med. chir. Trans.* LXI. 1878), and WELLER (*Arch. f. Psych.* 1879) all agree in stating that in **hydrophobia** circumvascular

extravasations, some of them hæmorrhagic, are found in the central nervous organs. BENEDIKT, KOLESSNIKOW, GOWERS, and WELLER also discovered circumvascular hyaline and granular coagulated masses formed from the extravasated elements of the blood, together with venous thromboses (BENEDIKT), and patches of 'granular' degeneration. FOREL was not able to verify these observations.

LANGHANS (*Virch. Arch.* vol. 64) found in the cord in cases of **tetany** certain circumvascular patches of cellular infiltration. NAUWERCK in a recent case of **chorea** minor with endocarditis observed small patches of inflammation situated chiefly in the medulla; these were combined with certain degenerative changes in the brain and cord. Myelitis is said to occur among the Kabyles in North Africa as a result of eating the pulse of *Lathyrus cicera*; see Art. 648, and MARIE (*Progrès médical* 1883), PROUST (*Bulletin de l'acad. d. méd.* XII. 1884).

The number of white blood-cells usually present in the brain (Duke KARL THEODOR of Bavaria, *Virch. Arch.* vol. 69) is increased in typhoid (POPOFF), but not necessarily owing to inflammation. Sometimes, though rarely, disseminated encephalitis is associated with typhoid.

STEUDENER (*Beit. z. path. Anat. d. Lepra mutilans* 1865), NEUMANN (*Skin diseases*, trans. by PULLAR, London 1871), TSCHIRJEW (*Arch. d. physiol.* 1879), and LANGHANS (*Virch. Arch.* vol. 64) found inflammatory foci in the cord in connection with anæsthetic leprosy. See also STURGE, *Brain* VII. 1885.

ERB and others affirm that in infantile spinal paralysis the inflammatory disturbance extends over the whole of the anterior columns, reaching its greatest intensity only at certain parts, and the wide-spread initial paralysis corresponds with this view of the case. After weeks or months however only circumscribed changes can be demonstrated, the extent of which varies with the extent of the persistent paralysis. When certain muscles only are paralyzed, certain spots only of the anterior horns are found to be degenerate.

References on myelitis:—CHARCOT, *Diseases of the nervous system* London 1880; LEYDEN, *Klinik d. Rückenmarkskr.* 1874–76, *Zeitschr. f. klin. Med.* I., *Arch. f. Psych.* VI.; HAMMOND, *Diseases of the nervous system* London 1876; ERB, *Ziemssen's Cyclop.* XIII.; SCHULTZE, *D. Arch. f. klin. Med.* XX., *Virch. Arch.* vol. 68; DUJARDIN-BEAUMETZ, *De la myelite aiguë* Paris 1872; WESTPHAL, *Arch. f. Psych.* III., IV. (1874); HAYEM, *Arch. de Physiol.* VI. (1874); LAVERAN, *ibid.* VII. (1875); BAUMGARTEN, *Arch. d. Heilk.* XVII.; HAMILTON, *Quart. Journ. of micro. science* 1875; TURNER, and HUMPHREYS, *Trans. Path. Soc.* XXX. 1879 (recent cases of poliomyelitis); DAMASCHINO and ROGER, *Gaz. méd.* 1871 (ditto); BARLOW, *On regressive paralysis* London 1878; ALTHAUS, *Infantile Paralysis* London 1878; ANGEL-MONEY, *Trans. Path. Soc.* XXXV. 1884; DRUMMOND, *Brain* VII. 1885; KRAUS, *Poliomyelitis apter. acuta* In. Diss. Tübingen 1882; SAHLI, *D. Arch. f. klin. Med.* XXXIII.; ETTER, *Corresp. f. Schweiz. Aerzte* 1882 (acute bulbar myelitis); LANGE, *Hosp. Tidende* 1868 (ditto); LEYDEN, *Arch. f. Psych.* VII. (ditto); LICHTHEIM, *D. Arch. f. klin. Med.* XVIII. (ditto); EISENLOHR, *Virch. Arch.* vol. 73; VON VELDEN, *D. Arch. f. klin. Med.* XIX. (disseminated myelitis); ENGELKEN, *Path. d. acuten Myelitis* In. Diss. Zurich 1867 (ditto); DRESCHFELD, *Lancet* 1, 1882 (ditto).

LEYDEN (*Arch. f. Psych.* VIII. 1877, *Charite-Annalen* III.) produced myelitis in dogs by injecting liquor arsenicalis (Fowler's solution) into the lumbar cord, and showed that the affection might terminate in cicatrization, sclerosis, cyst, or in simple rarefaction or loosening of the tissue. He thought that disseminated multiple sclerosis was the result of a disseminated myelitis or encephalitis. Clinically the term myelitis is used in a sense much wider than that to which we have restricted it. Thus poliomyelitis is used to describe conditions which are not

inflammatory, such as ischæmic and hæmorrhagic softening, simple atrophy, and multiple sclerosis of the gray matter. Secondary and primary tract-degenerations, ischæmic and hæmorrhagic softening, degeneration from pressure and contusion of the white matter of the cord or medulla oblongata, are all classed as myelitis. This may be convenient, but the pathologist is bound to be more discriminating. Even if it is not always possible in the post-mortem room to determine with certainty the manner in which a given change, say a patch of sclerosis, was initially induced, this is no reason for declining to classify such changes according to their mode of origin.

The terms acute and chronic progressive bulbar paralysis, anterior poliomyelitis, infantile spinal paralysis, atrophic spinal paralysis, transverse myelitis, leukomyelitis, protopathic and secondary spinal muscular atrophy, spastic spinal paralysis or paraplegia, and so on, are intended to express the character of the clinical symptoms and the seat of the lesion in the several maladies: for the most part however they fail to indicate or at least to indicate correctly the nature of the morbid process.

On acute polioencephalitis:—STRÜMPELL, *Deut. med. Woch.* 1884, *Jahrb. f. Kinderheilk.* XXII. 1885, *London Med. Record* 1885; GAUDARD, *L'hémiplégie infantile cérébrale* In. Diss. Geneva 1884; RANKE, *München. med. Woch.* 18, 1886. WOLFENDEN, *Practitioner* XXXVII. 1886.

CHAPTER XCVI.

TUBERCULOSIS AND SYPHILIS.

660. **Tuberculosis** of the central nervous organs and their membranes is in most cases embolic in origin, though the disease may also extend by continuity from neighboring tissues, such as the bones.

When the tuberculous virus reaches the brain or cord by way of the blood-vessels a form of tuberculosis is set up which we may call **disseminated tuberculous meningoencephalitis** or **meningomyelitis.** Where the bacilli first lodge their irritative action gives rise to minute inflammatory foci (Fig. 279, *c e f*), which in the subarachnoid and pia mater and in the substance of the brain and cord are distributed chiefly along the course of the small veins, in part also amid the capillaries of the nerve-substance itself. The pial sheaths (*f*) of the vessels are at first the chief seat of the inflammatory infiltration of cells; presently however the process extends also to the adjacent tissues (*e*). In a short time the collections of cells form nodules (*d*) and nodular clusters (*a b*), or more rarely larger continuous patches (*k*).

Disseminated embolic tuberculosis of the brain and cord runs in general a somewhat rapid course, and proves fatal in a few weeks' time. In addition to the nodular eruption there is often wide-spread diffuse inflammatory exudation of a sero-purulent or fibrino-purulent character, the pus infiltrating the meninges and the brain-substance, and often accumulating in the ventricles. It is only in rare cases and these very chronic (Fig. 279) that diffuse exudation fails to accompany an abundant eruption of tubercles.

In the soft membranes the first visible sign of tuberculosis is the appearance of small gray nodules usually lying along the course of congested vessels. By and by they become larger, and the subarachnoid spaces are seen to contain a turbid yellowish-white pus-like exudation. When the choroid plexuses are invaded they too contain gray nodules, and are swollen and infiltrated with a turbid liquid. The ventricles are more or less distended with the like exudation; sometimes they are enormously dilated, and the brain-substance thereby so compressed that the convolutions are flattened and the subarachnoid liquid expressed, leaving the arachnoid surface dry.

The completely-developed tubercles in the nerve-tissue appear as little nodules, gray and translucent, or yellowish-white with a gray periphery.

Quite recent continuous patches of tuberculous infiltration have a red-dish tint, like other inflamed parts.

Tubercles may appear in any part of the meningeal or nervous tissu[e]. If growing near a vein they are seen to penetrate not only the adventiti[a] but the inner coats, until the lumen of the vessel appears closely bes[et] and encircled with the accumulated cells. The white blood-cells insid[e] the vessel are often arranged peripherally, and sometimes visibly disten[d] it.

Arteries running through tuberculous foci have first the adventiti[a]

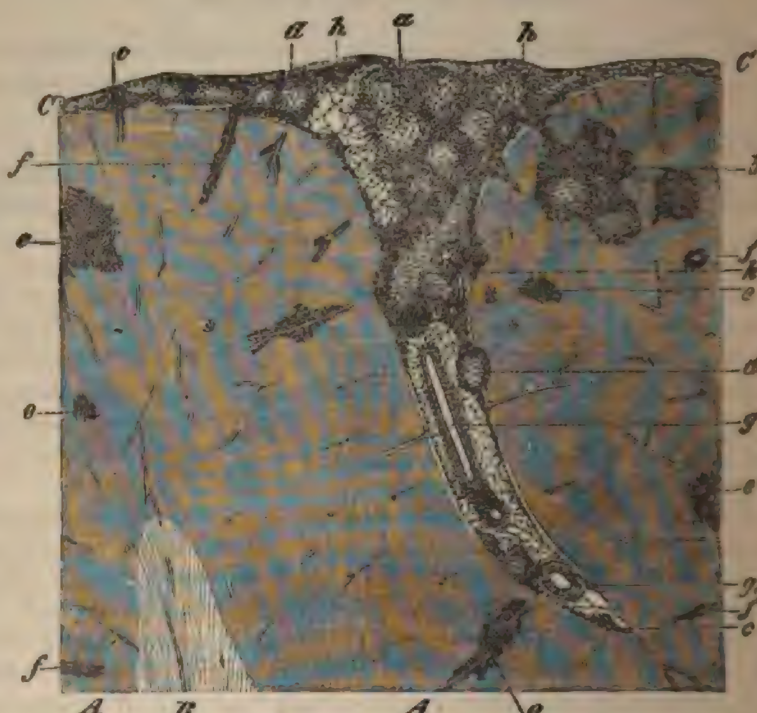

FIG. 279. CHRONIC DISSEMINATED TUBERCULOUS MENINGOENCEPHALITIS.

(Section hardened in Müller's fluid and alcohol, stained with alum-carmine, and mounted i[n] Canada balsam; × 10.)

A, cortex *B*, white matter *C*, meninges

a, dense fibro-cellular mass of tubercle in the subarachnoid tissue
b, tuberculous mass in the cortex
c, small tubercle in the pia mater
d, isolated tubercle in the subarachnoid tissue
e, circumscribed infiltration in the cortex, an early stage of tubercle
f, cellular infiltration of pial sheath of cortical vessels
g g_1, longitudinal and transverse section of a[n] artery
k, diffuse fibro cellular thickening of the sub-arachnoid tissue

invaded and infiltrated with cells; then the media and intima are at-tacked, especially the latter, which is sometimes so thickened by the in-filtrating cells that the lumen of the artery is encroached on and ob-

structed. If then the white blood-cells gather at the diseased spot and form a thrombus the occlusion becomes complete.

Tubercles in the brain or cord very rapidly undergo caseation, and only in chronic cases (Fig. 279) are large formative cells developed in appreciable numbers: in such cases the mature tubercles assume the large-celled coarse-textured appearance of those growing in lymphatic glands (Art. 342). When caseation begins in a tuberculous focus lying near a vessel of moderate size it generally extends to the walls and to the cellular contents of the vessel.

The commonest seat of embolic tuberculosis is about the basal branches of the sylvian artery: the disease is generally bilateral, though often more extensive on one side than on the other, and cases are not wanting in which it is unilateral. When the bacilli reach the arterial branches that pass upwards from the sylvian fissure to the surface of the cerebrum they give rise to more or less extensive meningitis of one or both sides of the convexity.

The territory of the arteries of the median plane of the cerebrum, cerebellum, medulla, and cord may in like manner be infected, and though this does not occur so frequently as in the case of the basal regions it is by no means rare.

When the eruption is abundant the chief mass of tubercle is usually to be found in the soft membranes of the brain and cord; but the nerve-substance hardly ever escapes entirely. The disease of the pia mater extends to the cortex as a diffuse cellular infiltration, leading to destruction of the nerve-elements, often preceded by a remarkable swelling of the axis-cylinders and of the ganglion-cells. In like manner the cranial and spinal nerves are attacked, the cellular infiltration reaching the pial sheaths, and thence spreading along the fibrous septa into the substance of the nerves, and often inducing degeneration of the nerve-fibres.

In addition to this meningeal invasion we frequently meet with tubercles growing directly in the deeper parts of the substance of the brain and cord: even in cases described as tuberculous meningitis the number of encephalitic and myelitic foci is at times very considerable; they are overlooked simply because they are apt to be very small.

If the bacilli lodge in a few branches only of the meningeal or cerebral arteries the first eruption of tubercles is scanty. But as the patient does not usually die at once, the tubercles grow and coalesce into large masses lying beneath the pia mater or in the midst of the nervous tissues. In the subarachnoid spaces and in the pia mater they form flat discoid masses of various sizes, and in the brain-substance rounded nodes, sometimes as large as a walnut or even a hen's egg. These are sometimes described as **solitary tubercles.** Their centres are yellowish-white and caseous, being sometimes firm and dense, sometimes soft and semi-liquid, rarely calcified. Their peripheral parts consist of grayish-red or semi-transclucent granulation-tissue, often enclosing typical miliary tubercles.

The larger tubercles are developed from the smaller by the continued growth of new granulomatous tissue, sometimes containing multitudes of giant-cells, sometimes none at all. It is remarkable that where the inflammatory process is going on the fibrous elements of the brain-tissue often undergo marked hyperplasia, and form thus a coarse fibro-cellular tissue. Tubercle-bacilli can be demonstrated both in the gray granulomatous zone and in the older portions of the growth.

Solitary tubercles are most frequently observed in the cerebellum and cerebral axis. They act like tumors on the neighboring tissues, giving rise to symptoms of pressure and to disturbance of the circulation both of blood and lymph. The other parts of the central organs may be entirely free from tubercle, though it often happens that tuberculous matter passes from the solitary nodes to the meningeal vessels and gives rise to disseminated and diffuse tuberculous meningitis. It is also of course possible for a fresh infection of the blood to take place, and in consequence a fresh embolic eruption of tubercles.

The situation of tuberculosis of the central nervous organs due to extension of tuberculous disease from contiguous parts is of course dependent on the seat of the primary affection. Tuberculous disease of the vertebræ infects the cord and its membranes, tuberculosis of the petrous bone extends in the first place to the temporal lobes and the basal aspect of the frontal lobe. Nodules appear in the affected regions, and these in time may grow into larger nodes. If the virus gain access to the cerebrospinal lymph-channels it may give rise to disseminated tuberculosis.

Many authorities (VIRCHOW, RINDFLEISCH, BIRCH-HIRSCHFELD, etc.) state that meningeal and cerebral tubercles lie usually in the adventitia of the arteries, and there form clusters of cells derived by multiplication from the endothelium of the lymphatics. They base this statement on the fact that in tuberculous meningitis collections of cells are found in the adventitia of the cortical arteries. This interpretation of the fact is however erroneous. The tubercles are developed from extravasated leucocytes and proliferous connective-tissue cells. The adventitia is affected and takes part in the proliferation only in a secondary way, and what has been described as a tubercle due to periarteritis of a pial vessel is in fact only a fraction of a tubercle growing near the vessel. In other inflammations of the pia mater and cortex we find like cellular infiltrations of the pial sheaths of the vessels, though it must not be overlooked that in tuberculous and syphilitic (Art. 661) inflammations the arteries take part in the cellular hyperplasia to a much greater extent than in other forms of inflammation. The like is true also of the endarteritic processes

References:—VIRCHOW, *Cellular Pathology* London 1860, *Krankh. Geschwülste* II. Frankfort 1856; WILKS, *Path. Anat.* London 1875; RINDFLEISCH, *Virch. Arch.* vol. 24, *Path. Histology* II. London 1873; HUGUENIN, *Ziemssen's Cyclop.* XII.; VON CAMPE, *Beitr. z. path. Anat. d. meningit. u. meningo-encephalit. Processe* Tübingen 1882.

661. **Cerebrospinal syphilis** usually makes its appearance some years after the disease has become 'constitutional,' that is to say,

simultaneously with the so-called tertiary symptoms: it is rarely an accompaniment of secondary symptoms. The characteristic morbid change is the formation of circumscribed inflammatory foci, or **gummata** as they are called, in the meninges and cortex, very rarely in the interior of the brain or cord. As a rule they lie in the pia mater and subarachnoid tissue of the base of the brain.

The first thing observed in the meninges is a small patch of inflammation, which soon leads to the formation of a gray or grayish-red semi-translucent or gelatinous knot of granulation-tissue (Fig. 280). In the earlier stages the tissue of the knot is extremely cellular (f), and contains a number of new-formed capillaries. As the process goes on some of the granulation-tissue becomes-fibro-cellular (d_1) and some undergoes

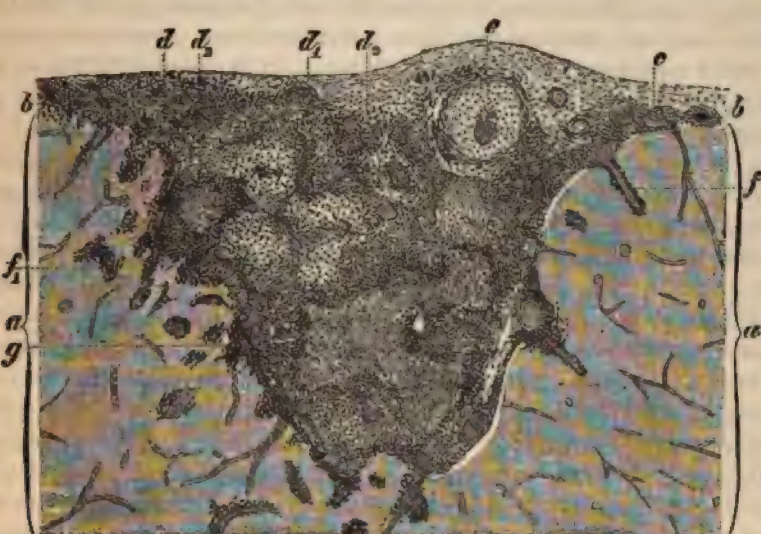

FIG. 280. GUMMATOUS SYPHILITIC MENINGOENCEPHALITIS.

(Section hardened in Müller's fluid and alcohol, stained in alum-carmine, and mounted in Canada balsam: × 15.)

a, cortex
b, pia mater
c, vein surrounded by cellular exudation
d, recent and cellular, d_1 fibro-cellular, d_2 caseous granulation-tissue
e, artery with thickened intima and infiltrated adventitia
f, cellular infiltration of the pial sheaths of the cortical vessels
g, diffuse infiltration extending into the cortical substance

caseation (d_2). The adjacent brain-substance seldom or never remains intact, the inflammation extending into the cortex along the pial sheaths of the vessels (f) and also directly (g). When arterial branches (e) pass through the granulomatous focus they are speedily infected, the adventitia, media, and intima becoming the seat of inflammation leading to cellular infiltration and fibro-cellular hyperplasia of the vessel-walls, according to the stage of the process. The intima (e) usually takes part

to a remarkable extent in this hyperplasia, the thickening being often so great that the vessel is much obstructed or even occluded outright. The latter event is most apt to occur when thrombosis accompanies the endarteritis.

Gummatous foci may be either single or multiple. The single foci are sometimes very small; HEUBNER indeed has shown that the specific inflammation may be limited to single spots on the arterial walls, and there lead to the thickening of the intima just described. Larger foci are however more frequent, and are described as nodes or gummata simply. In the earlier stages they are gray or grayish-red and soft, their form depending on the texture of the tissue in which they lie. On the surface of the brain they follow the course of the sulci and take their shape: in the sylvian fissure they are flat and elongated; about the base of the brain and the cord they have irregular forms. Sometimes about the basal meninges the syphilitic inflammation is more diffuse and not nodular. When it extends to the brain-substance and grows in size the diseased patch becomes more and more globular, and at times is as large as a walnut, though the periphery usually remains somewhat irregular. The same holds for the nodes which develop independently in the substance of the brain and cord.

The smaller foci can undoubtedly disappear by re-absorption: the larger ones become partly indurated and partly caseous. The caseation begins with the appearance of yellowish-white opaque spots, measuring from a few millimetres to some centimetres across according to the size of the node itself. When several such spots appear in the same node they give it a mottled appearance, until at length coalescing they form a yellow centre to the mass. Induration generally goes on simultaneously with caseation, though sometimes the latter is absent. It leads to scar-like thickening of the meninges, and to adhesions between the pia and dura mater. The coarse scar-tissue generally encloses caseous patches.

Where syphilitic inflammation is going on the nerve-elements of course perish; the process is frequently associated with ischæmic and hæmorrhagic softening of adjoining parts, consequent on the disturbance of the circulation induced by arteritis and compression. Occasionally these degenerative changes extend widely. Nerves passing through the inflamed region undergo inflammatory infiltration, and thereafter becoming enclosed and beset by coarse fibrous tissue they speedily atrophy and break down. Thus gummatous inflammation of the meninges at the lower end of the cord now and then leads to the enclosure of the greater number of the nerves of the cauda equina in a mass of granulation-tissue: this is presently transformed into a coarse cicatrix, and blended by adhesions with the dura mater forms a compact mass of scar-like tissue enclosing atrophied nerves and caseous patches. The same thing sometimes happens in the case of the cranial nerves.

Some nodes of the brain and cord which have been described as gummatous appear beyond a doubt to have been tuberculous. As the periphery and the neighborhood of these nodes do not always contain tubercles, before the discovery of the tubercle-bacillus it was not always easy to determine the nature of a given caseous mass. VIRCHOW has asserted that tuberculous nodes are rounded, while gummatous ones are irregular; but this criterion does not always hold good.

References:—VIRCHOW, *Virch. Arch.* vol. 15, *Krankhafte Geschwülste* II. 1869; LEON GROS and LANCEREAUX, *Des affections nerv. syph.* Paris 1861; ENGELSTEDT, *Die constitut. Syphilis* Würzburg 1861; WILKS, *Guy's Hosp. Rep.* IX. (1863); WAGNER, *Arch. d. Heilk.* IV. (1863); WESTPHAL, *Allg. Zeitschr. f. Psych.* XX. (1863); JAKSCH, *Prag. med. Woch.* 1864; LANCEREAUX, *Traité de la syphilis* Paris 1866 (trans. New Syd. Soc. II. London 1869); HEUBNER, *Arch. d. Heilk.* XI. (1870), *Die luetische Erkrank. d. Hirnarterien* Leipzig 1874, *Ziemssen's Cyclop.* XII.; GREENFIELD, *Trans. Path. Soc.* XXVIII., XXIX.; CHARCOT and GOMBAULT, *Arch. de physiol.* V. 1873; BRAUS, *Die Hirnsyphilis* Berlin 1873; BRUBERGER, *Virch. Arch.* vol. 60; WILKS and MOXON, *Path. Anat.* London 1875; BROADBENT, *Lancet* 1, 1874; BAUMGARTEN, *Virch. Arch.* vols. 73, 76, 86; VON RINECKER, *Festschrift z. Jubil. d. Würzburg. Universität* 1882; GREIFF, *Arch. f. Psych.* XII.; FOURNIER, *La syph. du cerveau* Paris 1879, *Leçons sur la syph.* (2d edition) Paris 1881; JULLIARD, *Etude critique sur les localis. spin. de la syph.* Paris 1879; WESTPHAL, *Charité-Annalen* I. (1876); GOWERS, *Hill and Cooper's Syphilis* London 1881; BUZZARD, *Lancet* 1, 1873 and *Brain* III. 1880, *Diseases of the nervous system* London 1882; DOWSE, *Syphilis of the brain and spinal cord* London 1881; ROSENTHAL, *D. Arch. f. klin. Med.* XXXVIII. 1886 (with numerous references).

CHAPTER XCVII.

TUMORS AND PARASITES.

662. Of the tumors occurring in the brain and spinal cord the **gliomata** (Art. 145, Fig. 40) claim our first notice. They are commonest in the cerebrum, more rare in the cerebral axis and in the cord: they lie usually close beneath the pia mater. In most cases the outer aspect of the brain-surface remains unaltered, the tumor appearing merely to cause enlargement and discoloration of the affected part, and perhaps some thickening of the meninges. It is seldom that the tumor takes the form of a definite protuberance.

On section the neoplastic mass consists sometimes of tissue not a little resembling pale or hyperæmic gray matter in tint and consistence: more commonly however the glioma is gray, grayish-white, grayish-red, yellow, or gelatinous in appearance, or mottled with all these tints and with spots of opaque white and of extravasated blood (Fig. 281 *b*); its consistence is in parts softer, in parts firmer than that of normal brain-tissue. Frequently it includes numerous vessels distended with blood, and of markedly larger calibre than the ordinary vessels of the part. When the hæmorrhages are numerous and extensive they may so stain and disguise the tissue that it looks like a patch of apoplectic extravasation. If the tissue is partly destroyed either by hæmorrhage or by softening the growth encloses cavities filled with turbid white or brown semi-liquid detritus.

Cerebral gliomata measure as much as 3 to 8 cm. across, or even more. The surrounding brain-substance is sometimes scarcely marked off from the substance of the tumor, sometimes is quite distinct and even visibly compressed: not infrequently it is softened and may contain cysts of disintegration. The ventricles are as a rule more or less dilated.

In the cord gliomatous tumors usually lie close to the central canal and spread thence posteriorly and externally. They are in general elongated, seldom globular, and may extend over a considerable length of the cord. Externally they give the cord a bulging or thickened appearance. Dilatation of the central canal and excavation of the growth itself are common (syringomyelia, Art. 635).

As we have mentioned in Art. 145 the tumor is made up of branched neuroglia cells, though the number and size of the cells present in dif-

ferent growths is subject to great variation. When they are small and scanty, and their ramifying fibrils numerous and closely felted, the texture is dense and firm: when the cells are large and numerous the tumor rather resembles a sarcoma.

The cells are in general uniformly scattered through the mass, but now and then they appear to lie in small clusters: multinuclear cells are common, especially in the peripheral parts of the growth.

The vessels are frequently much dilated (Fig. 41), and so abundantly developed that the tumor is fitly described as telangiectatic or angiomatous. The vessel-walls are often thickened and hyaline, and there is hyperplasia of the adventitia, the vessels being thus surrounded by a thick envelope of cellular and fibro-cellular tissue. Round the veins there may be accumulations of white blood-cells.

FIG. 281. ANGIOMATOUS GLIOMA.
(*Frontal section through the brain.*)
a, right hemisphere *b*, glioma in left hemisphere

The tumor grows by proliferation of the neuroglia and multiplication of its cells: at least this is as much as can be made out by examination of the growing margin. The nerve-fibres as they are encroached on perish, their axis-cylinders becoming notably swollen before they break down. The ganglion-cells and their nuclei also swell in a remarkable way, and become homogeneous and glassy in appearance. Later on they break down like the nerve-fibres, though it is sometimes surprising how long both elements persist.

When the glioma presses on the pia mater the connective-tissue cells of the latter undergo subdivision and multiplication, and a new-formation of fibrous tissue usually takes place. The gliomatous growth may ultimately extend into the meshes of the fibrous tissue. In ischæmic and

hæmorrhagic softening of the growth the cellular elements perish, partly by necrosis and partly by fatty degeneration. Sometimes peculiar protoplasmic lumps, with or without nuclei, are produced, apparently by coalescence of some of the cells. Stratified corpora amylacea also occur in the tumor-tissue.

Sometimes a mucous liquid forms abundantly in the interstices of a glioma and give it the appearance of loose mucous tissue: such tumors are described as **gliomyxomata.** Still more frequently the connective-tissue cells undergo so marked a proliferation that the tumor becomes a **gliosarcoma,** the neuroglia-cells increase greatly in number and size, and ultimately lose their typical characteristics. In other cases the vascular adventitia becomes abnormally proliferous, and the product of its overgrowth is at length so abundant that the gliomatous structure is overshadowed. Gliosarcoma is chiefly characterized by the multiform character of its cells; but the overgrowth just alluded to results in a spindle-celled neoplasm, the cells being arranged along the course of the blood-vessels: it is therefore described as **angiosarcoma.** Sarcomatous transformation in a cerebral glioma gives the tumor a marrowy or 'encephaloid' consistency, and marks it off more sharply from the surrounding brain-substance.

Sarcoma also occurs as an independent growth, unattended at first by any multiplication of neuroglia-cells. Spindle-celled and multiform-celled varieties are the commonest, and they are in general soft and marrowy. They are commonly rounded, sharply defined, of all sizes, and either single or multiple. So far as we at present know they develop from the pial sheaths of the vessels and in part from the neuroglia. Hæmorrhage and softening of the tumor are frequent. If it lies close beneath the pia mater it often invades that membrane. The surrounding brain-substance is generally softened, the meninges inflamed, and the ventricles dilated.

Small **angiomata** are not uncommon in the brain, though they do not form regular tumors but only small reddish foci, not unlike recent patches of inflammation. They are probably congenital (VIRCHOW), and are of the same nature as vascular nævi. There is simply telangiectasis of the blood-vessels, not cavernous metamorphosis of the tissue (Art. 149). GANGUILLET recently described as **cylindroma** a gelatinous-looking angioma of the lower end of the spinal cord: it was composed of vessels whose adventitia had become hyaline, and was beset with bulging hyaline outgrowths (Art. 163, Fig. 57).

Fibroma of the central nervous organs is rare: it forms rounded nodes, which in the cord and roots of the spinal nerves are sometimes multiple, especially in cases of multiple fibromata (neurofibroma) of the peripheral nerves (Arts. 154, 399, 670).

BIDDER mentions a case of **osteoma** in the corpus striatum; it measured several centimetres in diameter. MESCHEDE met with a bony

growth in the cerebral hemisphere of an epileptic. BENJAMIN describes a **lipoma** in the cerebrum.

Secondary growths, sarcomatous and carcinomatous, occur in the brain as in other organs: they usually form rounded nodes or nodules.

KLEBS maintains (*Viertelj. f. prakt. Heilk.* 125, 133) that the ganglion-cells take an active part in the production of gliomatous neoplastic cells, and HELLER (*Naturforscherversammlung in Freiburg* 1883) agrees with him. The author has gone over again his preparations of glioma, but is unable to find any ground for altering the view expressed in Art. 145. The ganglion-cells do indeed swell up considerably, and occasionally a binuclear cell can be seen; but that is all. As the tumor develops the ganglion-cells break down, and the clusters of neuroglia-cells afterwards found in their place are evidences merely that the latter have multiplied in their neighborhood.

As we remarked in Art. 651 it is not possible to draw a sharp line between glioma and sclerosis. This is especially true of the gliomatous growths occurring round the central canal of the cord, but it also holds of cerebral glioma. Sometimes part of the neoplastic change will appear to be essentially due to increase and induration of the connective tissue, while close by there is an unmistakable sharply-defined tumor.

Probably the smallest sarcomata of the central nervous organ hitherto described were observed some time ago by the author and Dr. ANDREAE in the cord of a lady who had suffered from some ill-defined disturbance of the innervation of the left arm: two nodules of spindle-celled sarcomata 2 and 3 mm. in diameter respectively were found in the left anterior horn of the cervical cord. The author has met with numerous small fibromatous nodules in the nerve-roots and the cord of a patient suffering from multiple fibroma of the peripheral nerves.

References:—VIRCHOW, *Krankhafte Geschwülste;* SCHÜPPEL, *Arch. d. Heilk.* VIII. 1867 (glioma and gliomyxoma of the cord); K. HOFFMANN, *Zeitschr. f. rat. Med.* XXXIV. 1869 (glioma; NEUMANN, *Virch. Arch.* vol. 61; TH. SIMON, *ibid.* vol. 61; GOLGI, *Cent. f. med. Wiss.* 1875; KLEBS, *loc. cit.;* GANGUILLET, *Beitr. z. Kenntniss d. Rückenmarkstumoren* Berne 1878; PETRINA, *Prager Viertelj.* 133, 134; ROTH, *Arch. de physiol.* 1878 (diffuse glioma of the cord); MESCHEDE, *Virch. Arch.* vol. 35; BIDDER, *ibid.* vol. 88; LEBERT, *Traité d'anat. path.* II.; CORNIL and RANVIER, *Man. Path. Hist.* I. London 1882; BENJAMIN, *Virch. Arch.* vol. 14 (lipoma of cerebrum); SCHULTZE, *Arch. f. Psych.* VIII. (periependymal angiomatous gliosarcoma of the cord); MEYER and BAYER, *Arch. f. Psych.* XII (relation of encephalitis to glioma); GERHARDT, *Festschrift d. Universität Würzburg* 1882 (glioma); OSLER, *Journ. of Anat. and Physiol.* XV. 1881 ('neuroma' of the brain, rather a heterotopia); REISINGER, *Virch. Arch.* vol. 98 (glioma of the cord); GLASER, *Arch. f. Psych.* XVI. (angiosarcoma of the cord); RENAULT, *Gaz. méd. de Paris* 1884 (cerebral glioma); BAIRD, *Les tumeurs du type nerveux, Arch. de physiol.* V. 1885.

663. The **tumors of the internal meninges,** the telæ choroideæ, and the lining membrane of the ventricles are chiefly of the mesoblastic or connective-tissue type; but epithelial or carcinomatous growths are also met with.

In the first place we have a group belonging to the **sarcomata** which form soft nodes, or less frequently broad flattened growths. Their section is marrowy, grayish-white or grayish-red in tint, sometimes almost

gelatinous. They are commonest about the base of the brain, more rare on its convexity, still rarer in the pia mater of the cord and telæ choroideæ of the ventricles; they are either entirely confined to the meninges or encroach somewhat on the nerve-substance.

So far as investigations have shown they originate partly in the adventitia of the vessels and partly from the (endothelial) cells which cover the fibrous trabeculæ of the arachnoid, subarachnoid, and pia mater. The new-formed cells become highly developed, and resemble the multiform epithelial cells of carcinoma. As they lie in a stroma composed of the meningeal tissues and form dense clusters in its meshes which look exactly like nests of cancer-cells, the tumor has the appearance of a carcinoma and is often so described. It is however strictly speaking an **alveolar sarcoma** (nested sarcoma) in type, and its structure and the grouping of its endothelial cells justify us in classing it with the endotheliomata (Art. 161).

Endothelioma appears to be the commonest growth met with in the soft membranes, but others also occur from time to time which must be classed as ordinary **sarcoma, myxosarcoma,** and **myxoma;** the latter is chiefly found in the pia mater of the cord.

The blood-vessels of sarcomatous and myxomatous growths sometimes develop in number and size until they transform these into what we must call angiosarcoma, angiomyxoma, and angiomyxosarcoma. The vessels are wide and thin-walled or narrow and thick-walled, and form networks and complicated coils. The intervascular tissue may be simply fibrous, or mucous, or sarcomatous. If it is scanty the tumor assumes the aspect of a simple **angioma.**

Fibroma, lipoma, and chondroma are rare; but they do occur in the meninges and ventricular plexuses, forming small nodular or lobulated tumors which compress the nervous tissue. Seated at the lower end of the cord they sometimes encircle and compress the nerves of the cauda equina, and lead to their atrophy and degeneration.

Another rare growth in the pia mater consists essentially of a coarse fibrous stroma containing wide cysts or cavities filled with lymph. It looks somewhat like a piece of œdematous tissue, but is distinguished therefrom by the abundant development in it of fibrous tissue, which marks it off sharply from the surrounding structure and forms thick septa between the cysts. It is thus a true neoplasm and might be described as cystic lymphangioma or **cystic fibroma.**

In all these growths, but especially in myxoma and in fibroma, calcification may set in, and alter the vessels or lead to an increase of the so-called **brain-sand.**

Calcareous plates are often formed in the otherwise unaltered pia mater; and in the ventricular plexuses the brain-sand may be so increased that the plexuses are visibly enlarged and turn an opaque white.

In tumors the like occurs, in combination with calcareous degenera-

tion of the vessels. When the accumulation of calcareous matter in the growth is very great we have what is called **psammoma.** The organic basis of brain-sand consists of flattened cells which cohere like the coats of an onion, become homogeneous and lose their nuclei, and then are calcified.

Carcinomata are found in the ventricles, and form soft tumors (Fig. 282 *a*), usually connected with the plexuses and originating in their epithelium or (more rarely) in that of the ependyma. The cancer-cells (Fig. 283 *a*) lying in a fibrous stroma are of the cylindrical or columnar type. By the outgrowth of the vascular stroma into papillæ the tumor sometimes assumes a papillomatous appearance (Fig. 283).

If as not infrequently happens the stroma undergoes partial mucoid degeneration (Fig. 283 *b c c*,) the tumor exhibits a very peculiar struc-

FIG. 282. PAPILLOMATOUS CARCINOMA OF THE CHOROID PLEXUS.

(*Frontal section through the third ventricle.*)

a, tumor with cysts
b, right optic thalamus
c, right lenticular nucleus
d, right internal capsule
e, right corpus striatum
f, left optic thalamus
g, left lenticular nucleus
h, left internal capsule
i, dilated left lateral ventricle

ture. The papillary outgrowths are transformed into cysts (Fig. 282, Fig. 283 *d*) separated merely by strings of epithelial cells (*e*), so that the epithelium forms a kind of stroma enclosing cysts formed of connective-tissue. **Epithelial pearls,** or concentric globes (*h*), are sometimes formed in the midst of the masses of epithelium, and look wonderfully like those met with in cutaneous cancers (Art. 172), while contrasting sharply with the cylindrical cells of the growth.

The tumor is usually confined to the ventricle, and leads to compression of the brain-substance (Fig. 282 *f g h*) and ventricular dropsy (*i*).

It may however invade the brain-substance, and give rise to secondary nodules (SPAET). It is not certain whether this form of tumor occurs as a primary growth in any other region, but it is quite possible that it may arise say about the anterior or posterior transverse fissure, or at the base of the brain near the infundibulum; it probably develops from aberrant germinal epithelium (Art. 181).

Cholesteatoma, or pearly tumor, is one whose mode of origin is not well understood; it is a growth characterized by the presence in it of white rounded 'pearls' with a nacreous lustre. It occurs chiefly in the dura mater of the base of the brain about the transverse fissures, but it is also found in the interior of the organ. The soft white mass of the growth consists mainly of epithelial scales like those of the epidermis. Most authorities assume its endothelial origin; but it seems more likely

FIG. [illegible]. PAPILLOMATOUS CARCINOMA WITH GELATINOUS DEGENERATION OF THE STROMA FROM THE THIRD VENTRICLE.

(*Section hardened in Müller's fluid, stained with alum-carmine;* × 25.)

a, fibrous stroma with blood-vessels
b, partially mucoid papilla
c, mucoid papilla coagulated by the hardening fluid
c_1, hyaline masses
d, cyst in degenerate stroma, with coagulated contents
e f, interpapillary strings and nests of cells
h, epithelial pearls

that its 'pearls' are derived from the epidermic epithelium of the medullary tube, and are thus connected by descent with the external surface. Moreover in rare cases (ZIEGLER) minute hairs have been found in the mass; and the situation of the tumor points in the same direction, for the places described are such that at the time of the development of the brain primitive epiblastic cells might well remain unelaborated, and form the rudiment of a neoplasm at a later stage (Art. 181).

Secondary growths of every kind occur in the meninges. It is worth noting that they sometimes spread far and wide in the subarachnoid spaces. Thus a metastatic cancer of the pia mater in the vertebral canal may in course of time encircle the greater part of the cord and infiltrate the cauda equina.

Of **animal parasites** the *Echinococcus* and *Cysticercus* are found in the brain and cord. The former takes the form of single or multiple hydatid vesicles of various size, which compress the nerve-substance and lead to softening. The *Cysticercus*, or measle, is commonest in the meninges of the brain, and appears either in the usual form as a small cyst with its scolex, or as the *Cysticercus racemosus*, a cluster of large lobulated usually sterile vesicles grouped like grapes around a parent cyst (Arts. 243, 245).

We may here make mention of some formations which are not strictly tumors, though in some points resembling them.

Aneurysms of the basilar arteries are very common, and reach a considerable size (see LEBERT, *Berl. klin. Woch.* 1866). **Varices** are developed chiefly in the pial veins of the cord, and sometimes become so large that they form vascular knots like hæmorrhoids, which compress the cord and lead to its degeneration. In the cerebral ventricles are found small nodules seated on the ependyma: they are simply compact **fibrinous deposits** which have become partially organized and contain formative cells and capillaries.

Many of the growths described as cerebral cancer or epithelioma have no claim to the title. EBERTH'S and ARNDT'S epitheliomata of the pia mater were cases of alveolar sarcoma; only those alveolar neoplasms in the development of which the epithelium of the medullary tube is concerned are to be reckoned as carcinomata.

CORNIL and RANVIER state (*Man. Path. Hist.* I. London 1882) that brain-sand arises from buds or off-shoots from the vessels, which are made up of flattened cells and presently become calcareous. They therefore describe the tumors which are characterized by the abundant presence of the sand as **angiolithic sarcomata.** It is doubtful whether all brain-sand is of this kind.

References on tumors:—VIRCHOW, *loc. cit.;* MÜLLER, *Virch. Arch.* vol. 8 (cholesteatoma), vol. 16 (melanoma); ROKITANSKY, *Handb. d. path. Anat.* II. (cholesteatoma, angioma); LEBERT, *Maladies cancéreuses* Paris 1851; PARROT, *Arch. de physiol.* 1869 (lipoma); MORRIS, *Trans. Path. Soc.* XXII. (angioma); WILKS and MOXON, *Path. Anat.* London 1875 (chondroma); ROBIN, *Journ. de l'anat. et de la physiol.* 1869 (endothelioma); J. ARNOLD, *Virch. Arch.* vol. 51 (cystic sarcoma telangiectodes); EBERTH, *ibid.* vol. 49 (endothelioma); ARNDT, *ibid.* vol. 51 (endothelioma); MESCHEDE, *ibid.* vol. 35 (osteoma); KLEBS, *loc. cit.;* EPPINGER, *Prager Viertelj.* 1875 (cholesteatoma); SPAET, *Primärer multipler Epithelkrebs d. Gehirns* Munich 1882; RINDFLEISCH, *Path. Hist.* II. London 1373; BERNHARDT, *Beitr. z. Symptom. u. Diagnost. d. Hirngeschwülste* Berlin 1881; GANGUILLET, *loc. cit.* (sarcoma of spinal pia mater); LEYDEN, *Klinik d. Rückenmarkskr.;* ERB, *Ziemssen's Cyclopædia* XIII.; FALKSON, *Virch. Arch.* vol. 75 (chondrocystosarcoma of choroid plexus); LACHMANN, *Arch. f. Psych.* XIII. (glioma of the filum terminale); DRESCHFELD, *Journ. of Anat. and Physiol.* XIV. 1879 (psammoma); BILLROTH, *Arch. d. Heilk.* III. (myxoma of pia mater of cerebellum); CHIARI, *Prag. med. Woch.* 1883 (cholesteatoma of dorsal cord); LANCEREAUX, *Traité d'anat. path.* II.

On *Cysticercus racemosus:*—VIRCHOW, *Virch. Arch.* vol. 18; HELLER, *Ziemssen's Cyclopædia* III.; MARCHAND, *Virch. Arch.* vol. 75, *Breslau. ärztl. Zeitschr.* 1881; ZENKER, *Ueb. d. Cyst. racem. d. Gehirnes* Erlangen 1882, *Henle's Beiträge* Bonn 1882; GRIESINGER, *Arch. d. Heilk.* III. 1862 (with references); FERBER, *ibid.*

On hydatids of the brain see the works of COBBOLD, DAVAINE, etc. (Arts. 245-248).

CHAPTER XCVIII.

THE DURA MATER, PINEAL BODY, AND PITUITARY BODY.

664. The **dura mater** is a stout fibrous membrane, closely adherent to the inner surface of the cranium, and dividing into two laminæ at the foramen magnum: one of these lines the vertebral canal, the other forms a sack-like investment for the spinal cord, the intervening space containing loose connective tissue, fat, and blood-vessels, in particular the venous plexuses.

Where the dura mater adheres to the bone it serves as its periosteum, and is liable to all the morbid changes that affect the periosteum of other bones. Certain special dangers also arise from its connection with the central nervous system, and these require separate consideration.

In the first place the dura mater is very frequently the seat of an inflammatory process known as **chronic internal pachymeningitis**, the result of various injurious agencies whose exact nature is not fully understood. The inflammation is usually hæmatogenous, and is associated either with inflammation of the pia mater and subarachnoid tissue on the one hand or with disease of the bones on the other. It is commonest in the cerebral dura mater, and may be unilateral and circumscribed, or bilateral and in scattered areas or generally diffused.

The first morbid sign is the appearance of very thin fibrinous deposits on the internal surface of the membrane: these consist of scanty liquid and cellular exudations from the dural vessels. After a time the fibrin becomes organized, or in other words pervaded by living cells and new-formed vessels growing as off-shoots from the inflamed capillaries. A delicate fibrous tissue is thus elaborated, which lines the dura mater as a semi-transparent vascular membrane.

The new-formed vessels have very thin walls and are particularly prone to bleed, the slightest disturbances of the circulation apparently sufficing to set up **hæmorrhage** by rupture or diapedesis. The consequence is that pachymeningitic membranes nearly always contain recent extravasations and pigmented deposits testifying to past hæmorrhage; this peculiarity has led to the affection being described as **hæmorrhagic pachymeningitis.** The extravasations are usually small, but now and then they are so extensive that they separate the false membrane from the dura, and form blood-cysts or **hæmatomata,** which may cause

grave compression of the brain. If the cyst gives way blood will of course escape into the subdural spaces.

Once the inflammation has begun it seldom attains to complete resolution and recovery. The extravasated matters are by degrees reabsorbed, but if they are at all abundant the process is very slow and imperfect, and their continued presence keeps up an irritation that induces renewed inflammation. New exudations and new membranes are thus produced, and at length a dense scar-like tissue results, which contains masses of pigment, fibrinous residues, and calcareous matters. Sometimes after resorption of a hæmorrhagic extravasation a localized collection of liquid appears between the dura and the cicatrized membrane; this has been called **hygroma of the dura mater,** or partial pachymeningitic hydrocephalus. In older denser and more fibrous membranes some of the vessels are gradually occluded by contraction, but other parts remain highly vascular, and fresh hæmorrhages keep up the chronic inflammation.

Pachymeningitic membranes do not usually adhere to the arachnoid; but when this happens the new-formed vessels pass down into the internal meninges.

There is also an **external chronic pachymeningitis** in which the changes are chiefly limited to the cranial surface of the dura mater: they consist of thickening of the membrane and absorption or hyperplasia of the bone. Moreover, the dura mater is frequently inflamed by extension of mischief from contiguous parts. Thus suppuration due to an infected wound of the skull may involve the dura mater (Art. 654); and otitis media or inflammation of the petrous bone or of the vertebræ or the interdural tissue frequently extends to this membrane. When suppuration takes place the dura has a discolored yellowish-white or grayish-yellow appearance: if the suppuration is preceded by hæmorrhage the tint may be grayish-green or brown.

Tuberculosis arises as a concomitant of embolic tuberculous leptomeningitis or of tuberculous bone-disease. The inner surface of the dura is beset with disseminated gray tubercles, while in more advanced stages pachymeningitic membranes containing tubercles, or large granulomatous vegetations, or caseous foci are found. The latter are commonest in connection with bone-disease, and then frequently affect both surfaces of the membrane.

In **syphilis** cellular infiltrations and granulations are formed in the dura mater, and lead in time to dense scar-like thickenings, which frequently enclose caseous masses. If the process goes on extensive adhesions are set up with the arachnoid and pia mater.

Most **tumors** of the dura mater are sarcomatous. The spindle-celled forms are the most frequent, but round-celled and multiform-celled types are also found. We also meet with **alveolar sarcomata** and **endotheliomata,** characterized by the formation of cell-nests and re-

ticulated strings of cells (Fig. 284 *cd*) within a fibrous **stroma** (*a*). These latter take the form of flattened or pedunculated fungoid outgrowths (*fungus duræ matris*), varying from the size of a pea to that of an apple, which grow inwards and indent the surface of the brain or cord. On the outer aspect of the dura they erode and even perforate the bone by continuous pressure and consequent atrophy. They are commonest within the cranium, being indeed rare in the spinal canal. The pedicle sends out root-like processes of cells into the substance of the dura mater, from which the growth evidently originates. The endothelium of the lymphatic vessels furnishes the characteristic clusters and strings of cells, and the latter are often excavated (*d*) in a way that immediately suggests the parent vessel. This appearance is visible chiefly in the recent parts of the growth, the older parts showing merely

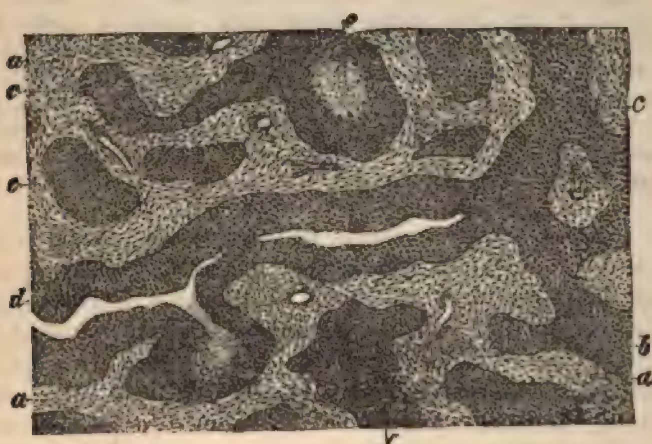

FIG. 284. ENDOTHELIOMA OF THE DURA MATER.

(*Hardened in Müller's fluid, stained with hæmatoxylin, and mounted in Canada balsam :* × 25.)

a, fibrous stroma
b, group of round-cells
c, nests and strings of cells derived from the endothelium of the lymphatic vessels
d, tubular tract of endothelial cells
e, fatty degeneration of a cellular mass
f, mass of endothelial cells, on the right side passing gradually into the fibrous stroma

a diffuse cell-growth which passes gradually into the structure of the fibrous tissue. When tumors of the dura mater become very vascular they may assume some of the characters of **angioma**; if the vessels calcify and give rise to an abundant production of brain-sand the growth becomes a **psammoma.**

Fibroma is on the whole rare, but it may occur in any part of the dura mater, forming rounded tumors; **lipoma** is very rare.

Enchondroma is not infrequently met with in the form of small gelatinous nodules about the back of the sella turcica and basilar portion of the occipital bone; the tumor originates in residual unossified frag-

ments of the cartilaginous synchondrosis between this bone and the sphenoid.

Osteoma occurs chiefly in the cerebral dura mater, and most frequently about the falx cerebri. The growth appears as a plate of bone of irregular form with spinous and ridge-like processes.

Of secondary or **metastatic growths** in the dura mater carcinoma is the most usual.

References on pachymeningitis:—VIRCHOW, *Würzburg. Verhandl.* 1856; SCHUBERG, *Virch. Arch.* vol. 16; KREMIANSKY, *ibid.* vol. 42; WEBER, *Arch. f. Heilk.* I. 1860 (hæmatoma); LANCEREAUX, *Arch. générales de méd.* 1862–63, *Traité d'anat. path.* II.; WILKS, *Med. Times and Gaz.* 1, 1868; RINDFLEISCH, *Path. Hist.* II. London 1873; SPERLING, *Cent. f. med. Wiss.* 29, 1871; PAULUS, *Verkalkung und Verknöcherung d. Hämatomes d. Dura Mater* Erlangen 1875; HUGUENIN, *Ziemssen's Cyclop.* XII.

On tumors of the dura mater:—ROKITANSKY, *Lehrb. d. path. Anat.* II.; ROBIN, *Recherches anat. sur l'epithéliome des séreuses, Journ. de l'anat.* 1869; LEBERT, *Virch. Arch.* vol. 3; ARNOLD, *ibid.* vol. 52; RUSTIZKY, *ibid.* vol. 59; BIZZOZERO and BOZZOLO, *Wiener med. Jahrb.* 1874; SCHÜPPEL, *Arch. d. Heilk.* X. (1869); VIRCHOW, *Die Entwickelung d. Schädelgrundes* 1857 (ecchondrosis of the basi-occipital); LUSCHKA, *Virch. Arch.* vol. 11 (ditto); ZENKER, *ibid.* vol. 12 (ditto); LANCEREAUX, *Traité d'anat. path.* II.

665. The hypophysis cerebri or **pituitary body** is seated in the sella turcica, and is composed of two lobes: the anterior consists of a fibrous stroma enclosing numerous round and oval follicles filled with epithelial cells, the posterior of vascular connective tissue containing cell-like clusters of fat-granules. At the junction of the two lobes the tissue is very vascular, and contains cavities lined with ciliated columnar epithelium (WEICHSELBAUM).

Cystic degeneration and hyperplastic overgrowth of the anterior lobe are not uncommon, the cysts usually containing colloid masses. This transformation is called **adenoma** of the pituitary body (WEIGERT), and the growth sometimes reaches the size of a hen's egg. It of course protrudes more or less from the sella turcica, presses on the adjoining brain-substance, or into the ventricles (ZENKER), and sometimes leads to atrophy of the underlying bone.

According to WEICHSELBAUM the ciliated cavities are very apt to undergo cystic change, the cysts containing homogeneous or granular matter secreted by the epithelium.

After adenoma the commonest growths are **carcinoma and sarcoma** (KLEBS), which also take the form of nodose swellings. WEICHSELBAUM has described a pair of small lipomata in the posterior lobe, and WEIGERT a teratoma.

The pituitary body may be inflamed in connection with disease of the neighboring parts: tubercles and gummata are however rare in this situation (WEIGERT).

The **pineal body** consists of fibrous tissue enclosing a number of more or less spherical follicles, each containing a reticulate structure of epithelial cells, a number of rounded cells with slender processes (TOLDT), and a quantity of brain-sand.

The most frequent pathological changes observed in this organ are —abnormal increase of the quantity of brain-sand (psammoma), hyperplastic enlargement (so-called glioma), and cystic degeneration (hydrops cysticus); it may participate in inflammations of the adjacent structures. The author once found in it a tumor as large as a pigeon's egg, consisting essentially of blood-clot (hæmatoma).

References on the pituitary body: VIRCHOW, *Die krankhaften Geschwülste;* ZENKER, *Virch. Arch.* vol. 13; WAGNER, *Arch. d. Heilk.* 1862; WEIGERT, *Virch. Arch.* vol. 65; WEICHSELBAUM, *ibid.* vol. 75; RIBBERT, *ibid.* vol. 90; KLEBS, *Viertelj. f. prakt. Heilk.* 125; BECK, *Zeitschr. f. Heilk.* IV. 1883 (teratoma); BERNHARDT, *Beiträge z. Sympt. u. Diagnostik d. Hirngeschwülste* Berlin 1881.

SECTION XII.

PERIPHERAL NERVOUS SYSTEM.

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PERIPHERAL NERVOUS SYSTEM.

CHAPTER XCIX.

STRUCTURE OF PERIPHERAL NERVES.

666. The peripheral nervous system is composed of **nerves** and **ganglia,** together with certain **terminal organs.** The nerves consist essentially of medullated and non-medullated fibres: in the ganglia there are similar nerve-fibres and associated ganglion-cells.

A **medullated fibre** is a long cylindrical structure, the axis being occupied by the so-called **axis-cylinder.** During life the latter is homogeneous and enclosed in a sheath of myeline (**medullary sheath**), and this again in a delicate fibrous envelope—the primitive sheath, neurilemma, or **sheath of Schwann.** The medullary sheath is interrupted at intervals by the **nodes of Ranvier:** at these points the axis-cylinder is covered only by the sheath of Schwann, and chiefly through them is its nutrition kept up. Each nerve-fibre is thus subdivided into segments of 1 to 2 mm. in length; each segment has about its middle a nucleus lying close to the sheath of Schwann, and on the inner side of the sheath close to the nucleus is a thin layer of protoplasm. External to the sheath of Schwann is a fibrillar sheath (AXEL KEY and RETZIUS), which also contains nuclei and a scanty protoplasm.

The **non-medullated fibres** possess an axis-cylinder with a primitive sheath containing nuclei at intervals.

Both kinds of fibres unite to form nerves of various degrees of thickness: the nerves from the brain and cord consist chiefly of medullated fibres, those of the sympathetic system chiefly of non-medullated fibres.

The smaller nerves consist of a single bundle of nerve fibres, the larger nerves of a certain number of bundles.

Each bundle (Figs. 286, 288 *c*) is surrounded by a fibrous envelope or **perineurium:** in a large trunk several such bundles are enclosed in a perineurium (Fig. 288 *a*), each of them being surrounded by an **epineurium** (*b*) of loose connective tissue, often containing fat-cells. Septa pass from the perineurium between the bundles (Fig. 286), and subdividing into finer fibres surround the individual nerve-fibres with an **endoneurium.** The blood-vessels of the nerve-trunk run in these fibrous envelopes. At the peripheral ends the axis-cylinders break up into primitive fibrils, and these terminate in the various peripheral end-organs.

In the course of some of the nerves (especially of the sympathetic)

are one or more clustered groups of ganglion-cells: when these are large enough to be easily visible they are called **ganglia.** The cells and fibres of such a ganglion lie in a fibrous stroma whose elements are in direct continuity with the fibrous structures of the corresponding nerve.

The **morbid changes** occurring in the nerves affect partly the nervous elements, partly the fibrous framework. In many respects the changes correspond to those affecting the central nervous system, but they also offer remarkable peculiarities of their own.

CHAPTER C.

ATROPHY AND DEGENERATION.

667. The degenerative processes which lead to **atrophy** and disappearance of the peripheral nerve-fibres and ganglion-cells correspond in their general course with the like processes in the brain and cord.

In the first place fibres and cells may gradually dwindle and waste away without undergoing any appreciable change of structure. More frequently however the destruction is speedier and accompanied with the various evidences of disintegration so often observed in the central organs.

In the **medullated fibres** there appears first a turbidity and then a splitting up of the medullary sheath, leading to the formation of large and then of smaller fragments and droplets of myeline, until the whole sheath is reduced to globules or particles. The axis-cylinder and its primitive fibrils may in like manner break up into small fragments (Fig. 285 *c*), or swell up and become liquefied; though it must be remembered that the axis shows itself more resistant towards many kinds of injury than the medullary sheath.

The sheath of Schwann usually remains intact, and even the so-called nerve-corpuscles or nuclei of the several segments persist also (Fig. 285 $d\ d_1\ d_2$). When the medullary sheaths break up, extravasated leucocytes pick up the products of disintegration and form fat-granule cells which lie within the primitive sheaths or in the fibrous envelopes. Sometimes the cells of the connective tissue also become fatty.

The single or clustered ganglion-cells occurring in the course of the nerves perish by swelling and liquefaction, by fatty change, or by simple atrophy.

A medullated nerve which has lost its medullary sheath shrinks in volume and looks gray and translucent: if it is at the same time vascular its tint is grayish-red.

The exact manner and extent of the degeneration of the nerve-elements depends on the nature of the injurious or destructive agent which is at work; though in all degenerative processes there is one feature which is constant, namely the prompt extension of the change over all the portion of the nerve to the distal side of any point at which the axis-cylinder is completely interrupted.

Such an interruption is most quickly and most completely effected by **section of the nerve**, and thus in the investigation of peripheral degeneration such intentional or unintentional section plays the chief part. At the cut surfaces of a nerve there quickly appears a button-like protrusion and swelling of a gray or grayish-red tint, together with some gelatinous exudation. In a day or two the segments of the peripheral portion become less refractive, and turbid, and by the third day the medullary and primitive sheaths are deeply indented at the nodes. On the fourth to the sixth day the medulla breaks up into large drops of myeline, and in a few days more there is nothing of it left but droplets and granules of detritus which are ultimately absorbed.

The axis-cylinder speedily becomes almost or altogether invisible, and perishes partly by swelling and vacuolation, partly by breaking up into fragments.

In simple uncomplicated section of the nerve the proximal or central end degenerates for a small distance only from the wound, the change stopping at the first or second node of Ranvier. Only when the nerve-end is bruised or otherwise inflamed do some of the bundles degenerate for a greater distance. In such a case the primitive sheath of the degenerate fibres contains a large number of extravasated leucocytes which in simple section are seldom or never very abundant.

Severe crushing or pinching and abiding compression (as from a tumor or a shrinking cicatrix) of a nerve have an effect similar to section, the latter leading to anæmic necrosis or degeneration of the compressed portion. The difference is chiefly in the fact that the interruption is not at once complete, but affects the several strands or bundles in succession.

Disease of the anterior horns of the cord and of the motor roots leading to destruction of motor ganglion-cells or nerve-fibres are, like other interruptions of the conducting tracts, followed by peripheral degeneration: but it must be kept in mind that when the destruction of the ganglion-cells is more gradual the corresponding atrophy of fibres is not so rapid, the medullary sheath wastes by degrees (Fig. 285 *b*), and within one and the same bundle we may find fibres that are sound, others partially atrophied (*b c*), and others totally destroyed (d_1 d_2).

A second frequent cause of degeneration of the nerves is primary and secondary **neuritis**, due to traumatic or infective inflammation of the connective-tissue framework (Art. 669), which leads to disturbance of the circulation and nutrition of the nerve or to direct compression of it. Sometimes too hæmorrhages give rise to injurious pressure on the nerve-fibres.

Lastly, motor nerves atrophy when their **muscles** are long **disused** (FISCHER), the atrophy being however confined to the peripheral parts: there is no ascending atrophy of such nerves to any extent comparable with the descending atrophy.

Occasionally we meet with local or multiple peripheral degenerations of which we cannot with certainty discover the cause. Thus the **vagus** is subject to degenerative changes without any apparent compression, inflammation, or other injury. BLASCHKO describes a wide-spread fatty degeneration of Auerbach's and Meissner's plexuses in the intestines.[1] The **multiple neuritis** of some authors (Art. 669) is in fact of the nature of degenerative atrophy.

In such isolated degenerations we must assume that some disorder of the circulation (due *e. g.* to change in the vessels or change in the blood) is at work. Thus **lead-poisoning** gives rise not only to degeneration of the muscular nerves (LANCEREAUX, GOMBAULT, FRIEDLÄNDER, etc.) but also to change in the intestinal plexuses. When the nerve-changes are acute and accompanied by febrile disturbance it is probable that

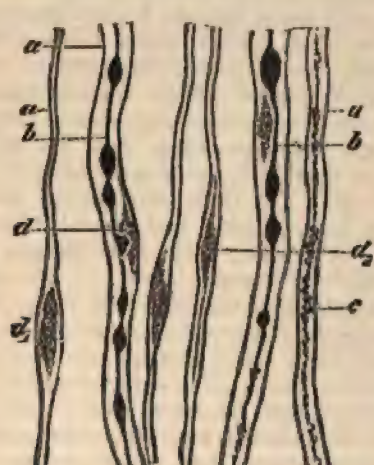

FIG. 285. ATROPHY OF MOTOR NERVES IN ANTERIOR POLIOMYELITIS.

(*Treated with Müller's fluid and perosmic acid, and teased out in glycerine* : × 200.)

a, sheath of Schwann
b, axis-cylinder with adherent drops of myeline
c, axis-cylinder breaking up
d, uninuclear,
d_1, multinuclear,
d_2, bipolar cell within the sheath of Schwann

infection of some kind is in question. R. MAIER showed experimentally that in chronic lead-poisoning the submucous and myenteric ganglion-cells become turbid, lose their nuclei, break into fragments, and disappear, while the connective tissue about them is simultaneously increased.

According to KEY, RETZIUS, S. MAYER, and KORYBUTT-DASZKIEWICZ, degenerative and regenerative changes take place normally in peripheral nerves; and many filaments hitherto assigned to the fibrous sheaths or the fibres of Remak are simply degenerate or nascent nerve-fibres.

The drops of myeline in degenerate nerves are stained black by perosmic acid

while the granular matters are unstained: S. MAYER infers from this that the nerve-substance breaks up into fatty and albuminoid component elements.

As to the exact fate of the axis-cylinder of the peripheral end of a cut nerve there is still some uncertainty, notwithstanding the numerous investigations that have been made: there is no question as to the medullary sheath. WALLER, EULENBURG, LANDOIS, HJELT, RANVIER, BENECKE, COSSY and DÉJÉRINE, TIZZONI, LEEGARD, VANLAIR, FALKENHEIM, and others state that the axis-cylinder degenerates; SCHIFF, PHILIPPEAU, KORYBUT-DASZKIEWICZ, ERB, CHARCOT, WOLBERG, and others maintain that it persists intact. In the text we have adopted the former account. After loss of the ganglion-cells in the anterior horns of the cord the axis-cylinders of the motor fibres, and after section of a peripheral nerve those of all the fibres, degenerate.

References on degeneration and regeneration of nerves after section:—WALLER, *Müller's Arch.* 1852, *Comptes rendus* 1851–52; SCHIFF, *ibid.* 1854; PHILIPPEAU and VULPIAN, *ibid.* 1859; HJELT, *Virch. Arch.* vol. 19; REMAK, *ibid.* vol. 23; EINSIEDEL, *Ueb. Nervenregener. nach Ausschneidung eines Nervenstückes* Giessen 1864; LAVERAN, *Rech. exp. sur la régénér. d. nerfs* Strasburg 1867; EULENBURG and LANDOIS, *Berl. klin. Woch.* 1864–65; ROBIN, *Journ. d. l'anat.* 1868; NEUMANN, *Arch. d. Heilk.* IX. (1868); ERB, *D. Arch. f. klin. Med.* IV., V.; HERZ, *Virch. Arch.* vol. 46; VULPIAN, *Arch. d. physiol.* 1873–74; WEIR-MITCHELL, *Injuries of nerves* London 1872; LÉTIÉVANT, *Traité des sections nerveuses* Paris 1873; LEEGARD, *D. Arch. f. klin. Med.* XXVI.; BENECKE, *Virch. Arch.* vol. 55; RANVIER, *Leçons sur l'histologie du syst. nerv.* Paris 1878; COSSY and DÉJÉRINE, *Arch. de physiol.* 1875; ENGELMANN, *Pflüger's Arch.* XIII. (1876); BAKOWIECKI, *Arch. f. mikrosk. Anat.* XIII. (1876); COLOSANTI, *Arch. f. Anat. und Physiol.* 1878; GLUCK, *Virch. Arch.* vol. 72, *Arch. f. klin. Chir.* XXV., XXVI.; SANTI SIRENA, *Ricerce sperim. sulla reprod. d. nervi* Palermo 1880; TIZZONI, *Arch. p. l. sci. med.* III. (1878), *Cent. f. med. Wiss.* 1878, *Sulla patolog. d. tessuto nervoso* Turin 1878; S. MAYER, *Degen. und Regen. d. Nervenfasern* Prague, 1881; HOGGAN, *Trans. Path. Soc.* XXIII. (1880), *Journ. d. l'anat.* XVIII. (1882); GESSLER, *D. Arch. f. klin. Med.* XXXIII. (motor-nerve changes after section), *Die motor. Endplatte u. ihre Bedeut. f. d. periphere Lähmung* Leipzig 1885; NEUMANN, *Arch. f. mikrosk. Anat.* XIII. (1880), XVIII. (1885); VANLAIR, *Arch. de biol.* III. (1882); EICHHORST, *Eulenburg's Realencyclop. d. gesam. Heilkunde*, *Virch. Arch.* vol. 59; PEYERANI, *Biol. Centralb.* III. (1883); FALKENHEIM, *Zur Lehre von d. Nervennaht* In. Diss. Königsberg 1881; TILLMANNS, *Arch. f. klin. Chir.* XXVII.; BASCH, *ibid.*; WOLBERG, *Deut. Zeitschr. f. Chir.* XVIII., XIX. (1883); NICAISE, *Internat. encyclop. of surgery* III. London 1883; P. BRUNS, *Mitth. a. d. chir. Klinik* II. Tübingen 1884; CATTANI, *Arch. p. l. sci. med.* VIII. 1885 (nerve-stretching); HAYEM and GILBERT, *Modification du syst. nerv. chez un amputé*, *Arch. de physiol.* III. (1884).

The memoirs of VANLAIR, FALKENHEIM, TILLMANNS and WOLBERG include not only experimental researches of their own, but also summaries of published cases, and criticisms on previous methods of experiment: the subject of nerve-suture is also dealt with. WOLBERG'S paper is the most comprehensive on all points bearing on the main subject.

On nerve-degeneration from lead-poisoning and from undetermined causes:—LANCEREAUX, *Gaz. méd. de Paris* 1862, 1871; GOMBAULT, *Arch. de physiol.* V. (1873); DÉJÉRINE, *Gaz. méd. de Paris* 1879; ZENKER, *Zeitschr. f. klin. Med.* I. (1880); WESTPHAL, *Arch. f. Psych.* IV. (1873), VI. (1875); REMAK, *ibid.* VI. (1875); VULPIAN, *Mal. du syst. nerveux* Paris 1879; FRIEDLÄNDER, *Virch. Arch.* vol. 75; POPOW, *ibid.* vol. 93; R. MAIER, *ibid.* vol. 90; KUSSMAUL and MAIER, *D. Arch. f. klin. Med.* IX. (1872); EISENLOHR, *ibid.* XXVI.; BLASCHKO, *Virch. Arch.* vol. 94; DUMÉNIL, *Gaz. hebdom.* 1864; SCHULTZE, *Arch. f. Psych.* XIV.; MONAKOW, *ibid.*

X.; MORITZ, *Journ. of Anat. and Physiol.* 1880; BIRSDALL, *Amer. Journ. of neurology* 1882; NAUNYN, *Ziemssen's Cyclop.* XVII.

On atrophy from disuse:—FISCHER, *Deut. Zeitschr. f. Chir.* VIII. (1877); SIEGMUND MAYER, *Prag. med. Woch.* 1878.

CHAPTER CI.

REGENERATION OF NERVES.

668. **Union of severed nerves.** It has long been known that nerves which have been cut through, and whose function has been thereby completely abolished, are capable of repair, and in the course of weeks or months recover their conducting power. Recent surgery has utilized this fact, and seeks to bring about the speedier union and recovery of severed nerves by **suture** of their ends. Over fifty cases have already been published in which nerve-suture has resulted in more or less perfect restoration of function, and that not only when the wounds were recent but in some cases where suture did not take place till after the lapse of months or years from the time of injury.

The union and recovery of severed nerves has been often observed in animals as well as in men, and in recent years a large number of experiments have been made to throw light on the fact and on the histological process by which it is brought about. Unfortunately we do not yet fully understand all the steps of this process: opinions differ as to the fate of the peripheral end of a severed nerve (Art. 667), and it is therefore scarcely surprising that authorities are not agreed as to the details of **regeneration.** Hardly two of the multitude of writers on the subject take exactly the same view, and we are therefore unable to give an account of it which shall be wholly satisfactory.

When the functional continuity of a nerve is interrupted by section, crushing, compression, etc. various things may happen. The nerve-fibres only may be injured, the nerve remaining still macroscopically continuous; or it may be completely severed, the ends retracting some small distance apart, or becoming so widely separated that there is no possibility of their reuniting naturally. The regenerative process can be best followed in the second case, which is that most frequently observed experimentally, the parted nerve-ends being reunited by the intercalation of a new-formed piece of nerve.

The wound that severs a nerve is immediately followed by an inflammation, which leads to swelling of the cut ends, and the deposit of exudation between them. In the subsequent week or two granulations and cicatricial tissue are formed, while the central and peripheral ends undergo the changes referred to in Art. 667.

The [illegible]ion of the nerve-fibres begins a few days after the

operation (RANVIER) in the central end: RANVIER says at the very extremity of this end, VANLAIR at a distance of 1.5 to 2 cm. from it. EICHHORST observed the beginning of regeneration in the nerve of a rabbit on the fourteenth day after injury.

The first change is a swelling of some of the axis-cylinders in the outer parts (VANLAIR) of the nerve-bundles of the central end, and this is followed by subdivision of each into from two to five new axis-cylinders (RANVIER). The new cylinders grow in length, and form within the old sheath of Schwann whole bundles of new nerve-fibres (Fig. 286 *e*), which usually distend the lumen of the sheath and compress any persisting remnants of the older fibres (*f*). According to VANLAIR they sometimes burst the old sheath, and then either grow out amid the tissue

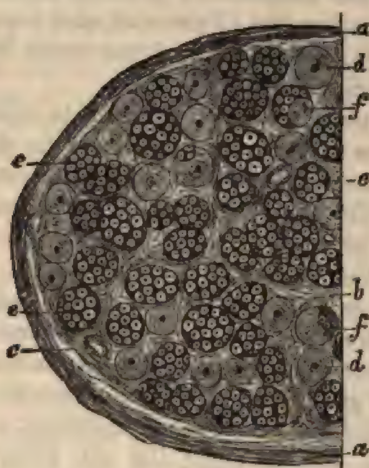

FIG. 286. CENTRAL END OF A NERVE-BUNDLE IN PROCESS OF REGENERATION.

(*From the median nerve 4 months after severance by a stab: hardened in Müller's fluid, stained with neutral carmine, and mounted in Canada balsam:* × 200.)

a, perineurium
b, endoneurium
c, blood-vessel
d, old unaltered nerve-fibre
e, bundle of new-formed nerve-fibres
f, new-formed nerve-fibres compressing an old fibre within the same sheath

of the endoneurium, or penetrate the perineurium of the bundles into the epineurium.

In this way at the extremity of the central end a large number of new fibres are developed. They consist at first of new-formed axis-cylinders surrounded by a protoplasmic nucleated sheath (VANLAIR), and presently they receive a homogeneous envelope of connective-tissue (*e*) formed at the expense of the protoplasmic sheath, and a thin medullary sheath which grows between the latter and the axis-cylinder. The perineurium of the bundles giving way and the new fibres thus dispersing as it were in the epineurium, the characteristic grouping of the nerve-fibres in

bundles is lost; the new fibres are more uniformly spread through the connective tissue, and the usually fatty epineural envelope assumes a striated fibrous appearance.

In this manner the re-formed and growing nerve enters the soft mass of granulations and cicatricial tissue that intervenes between the severed ends. When it reaches the peripheral end, some of whose fibres have meanwhile perished, certain of the new fibres enter the empty primitive sheaths (RANVIER), but the greater number penetrate the epineurium (VANLAIR) and perineurium and advance towards the peripheral end-organs. Others miss the peripheral end and run either alongside it or on a course of their own to the surface: many fibres too which leave the old track disappear and are lost in the tissues (VANLAIR). In the peripheral half of the intercalated cicatrix the nerve-fibres begin to gather once more into bundles (VANLAIR), and a perineurium forming round these, the whole thickness of the nerve by degrees assumes a nearly normal appearance.

These changes require weeks or months to complete: according to EICHHORST the fibres of the central end reach the cicatrix about the end of the first month, and in some three months the reunion is established.

It appears from the foregoing that the peripheral end does not itself regenerate, but is provided with nerve-fibres from the central end. VANLAIR describes the process as **neurotization**. It probably takes place in all cases of regeneration after severance, both when the nerve is actually cut through and when only the nerve-fibres and not the fibrous structures are interrupted. The difference is that in the former case the new fibres must grow through a certain amount of cicatricial tissue, while in the latter there is little or no granulation, and the axis-cylinders as they lengthen can directly enter the old fibres. Some authorities (GLUCK, WOLBERG, LANGENFELDT) state definitely that under favorable conditions very rapid union of the severed ends is possible, the function of the nerve being recovered in a very few days.

Even when the peripheral is so remote from the central end that direct union by nerve-tissue is out of the question, some attempt is still made at regeneration. The central end grows out (Fig. 286), but the axis-cylinders do not reach the peripheral end, and lose themselves in the cicatrix.

The so-called **amputational neuromata** (Art. 154) are of this nature; they are club-shaped enlargements of the severed nerve-ends occasionally met with in stumps which have healed after amputation. As they contain new nerve-fibres as well as connective-tissue they are doubtless due to an abortive attempt at regeneration in the nerve-stumps: when they include sensory fibres which are compressed or irritated by the cicatrix they are the source of very considerable pain. Similar traumatic neuromata now and then occur in the course of nerves which have been injured but not severed.

The statements of authors concerning the new-formation of the axis-cylinder in divided nerves are very discordant. WALLER, SCHIFF, RINDFLEISCH, CORNIL, RANVIER, EICHHORST, and others assert that it is due to longitudinal subdivision and growth in length of the old axis-cylinders. PHILIPPEAU, VULPIAN, REMAK, LEEGARD, NEUMANN, DOBBERT, DASZKIEWICZ, and others regard the new cylinder as derived from the peripheral end; LEEGARD believing that it arises from the nuclei of the neurilemma, REMAK from the uninjured and surviving cylinders, DASZKIEWICZ from the surviving segments of the old and partially degenerate cylinders, NEUMANN and DOBBERT from a protoplasmic mass produced by a chemical transformation of the medullary sheath and axis-cylinder. NASSE, GÜNTHER, SCHÖN and STEINRÜCK assert that the new cylinders grow from the old fibres of both ends: LENT, EINSIEDEL, WEIR-MITCHELL, BENECKE, and GLUCK, from the primitive sheaths of both ends; LAVERAN and HERZ refer their origin to the white blood-cells, HJELT and WOLBERG to the cells of the perineurium.

As the text shows we incline to the view of those who derive the new nerve-fibres from the old nerves of the central end. The subdivision of the axis-cylinder is the essential part of the process, though it is perhaps not impossible that a new-formation of nerve-fibres may start from the cells or nerve-corpuscles or nuclei on the sides of the sheaths of Schwann. At any rate it is remarkable how frequently in degenerating nerves we find these cells (Fig. 385 dd_1) swollen up and containing several nuclei: sometimes indeed they give off processes which much resemble axis-cylinders (d_1). Until we have more information on the subject however it is more probable that these cells form merely the sheaths for the new axis-cylinders. CATTANI asserts that new axis-cylinders are formed within the nucleated protoplasmic mass which he has observed filling the primitive sheath of degenerating nerves.

The hypothesis that nerve-fibres may grow from granulation-cells or from the connective-tissue cells of the perineurium, endoneurium, or epineurium, is contrary to all histogenetic analogy. The nerves throughout their length are originally outgrowths from the central nervous system (BALFOUR, HENSEN, HIS, KÖLLIKER, etc.), and it is extremely unlikely that in later life they can arise from indifferent connective-tissue cells: this would be at variance with all our experience on the subject of the regeneration of specific tissues. The authors who have made the assertion do not advance any convincing arguments in its favor.

Those who believe that after section of a nerve the axis-cylinders of the peripheral end remain intact assume that the ends of the severed cylinders reunite by the intercalation of a new piece of tissue. WOLBERG describes this as taking place by the growth of strings of spindle-cells from the epineurium. When the reunion does not take place till the medullary sheath disintegrates he speaks of the process as regeneration in the strict sense of the term. If reunion takes place before the sheath disappears he speaks of it as union by first intention, and distinguishes a mediate and an immediate variety. In the former the union is brought about by means of new-formed intercalary fibres, in the latter by direct adhesion of the severed ends of the cylinders and primitive sheaths. The existence of the mediate variety he claims to have experimentally proved. Such a union by first intention is very doubtful: GLUCK'S and WOLBERG'S experiments do not appear to prove it, and it is probable that mistakes have arisen from the rapid restoration of function that sometimes takes place by means of abnormal nervous anastomoses and supplementary fibres. The secondary or mediate union by means of intercalary fibres appears impossible, the cylinders of the peripheral end being already degenerate: and for the same reason the statements of GLUCK and others that a piece of nerve cut from one animal may become united to the two ends of a severed nerve in another must be regarded as resting on error.

CHAPTER CII.

INFLAMMATION OF PERIPHERAL NERVES AND GANGLIA.

669. **Neuritis,** or the inflammation of nerves, is characterized anatomically by the presence of an exudation in their fibrous framework. If the exudation is chiefly liquid and the blood-vessels are still filled, the inflamed nerve looks red, and swollen, and abnormally moist: if the exudation is cellular (Fig. 287) and the hyperæmia has disappeared there are no apparent signs of the affection, though any hæmorrhage that has taken place may be indicated by reddish or brownish-yellow discoloration.

In simple nerves the migrated leucocytes lie chiefly in the thicker trabeculæ of the endoneurium (Fig. 287 *d*) through which the vessels

FIG. 287. CHRONIC NEURITIS.

(*Hardened in Müller's fluid and alcohol, stained with hæmatoxylin and carmine, and mounted in Canada balsam:* × 150.)

a, normal thick nerve-fibre
b, normal fine nerve-fibre
c, endoneurium
d, blood-vessel, and trabeculæ of endoneurium infiltrated with leucocytes
e, leucocytes between the nerve-fibres
f, thickened endoneurium with small spaces devoid of nerve-fibres and a few thin fibres still persisting.
g, longitudinal section of a blood-vessel

run, though they may also pass in between the individual nerve-fibres (*c e*).

In compound nerves (Fig. 288) the exudation frequently lies almost entirely in the epineurium. The perineurium of the bundles and of the nerve generally is usually much less densely infiltrated.

Slight inflammations resolve without leaving any trace: severer attacks result in degeneration of some of the nerve-fibres. If the in-

flammation is suppurative or gangrenous the nerve rapidly breaks down and perishes, becoming of a dirty yellowish-white, gray, or grayish-green. The connective-tissue elements are however less vulnerable and long resist dissolution.

If the affection is chronic, degeneration of the nerve-fibres ultimately sets in, with the breaking up of some of the medullary sheaths. The axis-cylinders persist for a long time, though they too at length perish; and thus a certain number of the fibres disappear outright, the sheaths of Schwann collapsing (*f*). Wherever an axis-cylinder decays degeneration takes place all down the peripheral portion of that fibre (Art. 667). As the medullary sheaths break down the tissue of the nerve is beset with drops of myeline and granule-carrying cells.

In process of time the chronic inflammation leads to thickening and condensation of the connective tissue, and this with the atrophy of the nerve-elements gives the nerve by degrees the appearance of a fibrous cord. Whether the nerve as a whole is thicker or thinner than in health depends on the proportion between the fibrous hyperplasia and the nervous atrophy. Both in simple and in compound nerves the inflammation may and sometimes does extend over the whole cross-section. In compound nerves the separation of the bundles becomes less distinct, though it is not obliterated even when the atrophy and fibrous changes are very advanced. When the process has been accompanied by hæmorrhage the altered tissue is frequently pigmented.

Chronic neuritis accompanied by great fibrous hyperplasia has been called by Virchow **proliferous neuritis**: if it extends upwards or downwards we speak of it as ascending or descending neuritis respectively.

One of the commonest causes of neuritis is mechanical injury (cutting, bruising, etc.) by a wound or blow: the inflammation results in fibrous hyperplasia, but if it becomes septic suppuration or gangrene may set in.

Moreover the inflammatory process sometimes extends to a nerve from the adjacent tissues; thus nerves running through a wound may undergo granulation or even suppuration without having received any direct injury, and the like extension takes place in the case of other inflammations.

For example, it is extremely common for cerebrospinal nerves traversing an inflamed meninges to be themselves invaded by the inflammatory infiltration. And inflammations of the bones lead to indirect degeneration by compression or to direct inflammation of the nerves that traverse them. This also happens to nerves lying in the neighborhood of chronically inflamed or tuberculous lymphatic glands. It is not uncommon for instance for caseous glands in the neck, beside the trachea, or at the root of the lung, to press upon contiguous nerves, like the vagus and its branches, to irritate them into inflammation, and so to

bring about their degeneration. In the pelvis inflammations of the bladder or of the internal generative organs are apt to extend to the cellular connective tissue and so to the rich nerve-plexuses of that region.

These forms of neuritis are consecutive or secondary, but other forms occur in which the irritant inducing the inflammation is brought to the nerve directly by way of the blood or lymph. These irritants are so far as we know chiefly of an infective nature: thus in typhus (BERNHARDT), small-pox (JOFFROY), typhoid (NOTHNAGEL, LEYDEN, EISENLOHR), and diphtheria (OERTEL, CHARCOT, BUHL, DÉJÉRINE) we meet with simple or multiple neuritis, which we can only regard as direct results of the general infection.

Recently BAELZ and SCHEUBE have shown that the epidemic disease of India and Japan known as **beriberi** or **kakke** is characterized by the appearance of multiple neuritis: it has therefore been designated (BAELZ) as **panneuritis epidemica.**

It does not appear that there is any affection in Europe exactly corresponding to the Japanese *kakke*, but a form of multiple neuritis (LEYDEN) has more than once been described under the names of polyneuritis (PIERSON) and neuritis disseminata (ROTH). Whether this has any analogy to the infective disease, as PIERSON suspects, is still a very open question. Cold is spoken of by many as a cause of multiple neuritis, but probably in most cases some kind of infection or poison is at work. ROTH has shown that a purulent inflammation (as in parotitis) which involves a nerve-trunk may be the starting point of multiple neuritis.

Tuberculous and syphilitic inflammation affect chiefly the intracranial portions of cranial nerves and the spinal nerve-roots in connection with meningeal tuberculosis and syphilis respectively.

Little is known of tuberculosis or syphilis of the peripheral nerves. Foci of some size are most frequently observed in the optic nerve, and give rise to extensive tuberculous destruction. Elsewhere nerves are seldom involved except by extension of tuberculous inflammation from diseased glands.

Leprous inflammation is especially apt to attack the nerves, the disease being in fact chiefly characterized by its thus involving the peripheral nervous system: a particular form of leprosy is distinguished as *lepra nervorum anæsthetica*, or *lepra mutilans* (Arts. 131, 206, 392, 659, and HOGGAN, *Arch. d. physiol.* 1882). The settlement of the lepra-bacilli excites an intense inflammation, accompanied by cellular infiltration and followed by degeneration of the nerve-fibres and hyperplasia of the fibrous tissue. Fusiform thickenings and tuberosities of considerable firmness and size are thus produced in the course of the several nerves. The diseased tissue contains lepra-bacilli, some lying free and others being enclosed in cells.

We know little concerning the **inflammations of the ganglia:** they apparently occur under the same conditions as those of the nerves, and like them they are characterized by cellular infiltration, fibrous hyperplasia, and degenerative atrophy of the nerve-elements.

In severe cystitis and pyelonephritis and in inflammation of the internal generative organs in women paralysis of the lower limbs is sometimes a symptom. REMAK (*Med. Central-Zeitung* 1860) and LEYDEN (*Sammlung klin. Vorträge* 2, 1870) explain this as due to a progressive or wandering neuritis, which has been called **neuritis disseminata migrans** (LEYDEN). The experimental researches of WEIR-MITCHELL (*Injuries of nerves* London 1872), TIESLER (*Ueb. Neuritis* In. Diss. Königsberg 1869), FEINBERG (*Berl. klin. Woch.* 1871), KLEMM (*Ueb. neuritis migrans* In. Diss. Strasburg 1874), NIEDICK (*Arch. f. exp. Path.* VII. 1877), ROSENBACH (*ibid.* VIII.), and TREUB (*ibid.* X.) fail to confirm this explanation. It is much more likely that in the affections named the pelvic plexuses are compressed or directly inflamed by extension from the inflammation of the cellular connective tissue (pelvic cellulitis). See discussion by ADAMS and others (*Lancet* 2; 1880).

On multiple neuritis:—DUMÉNIL, *Gaz. hebdom.* 1864, 1866; LEYDEN, *Ueb. Reflexlähmung, Samml. klin. Vorträge* 2, 1870, *Charité-Annalen* V., *Arch. f. Psych.* VI., *Zeitschr. f. klin. Med.* I. 1880; CASPARI, *ibid.* V.; GRAINGER STEWART, *Edin. Med. Journ.* 1881; EICHHORST, *Virch. Arch.* vol. 69; JOFFROY, *Arch. de physiol.* 1879; EISENLOHR, *D. Arch. f. klin. Med.* XXVI.; MARCHAND, *Virch. Arch.* vol. 81; ERB, *Ziemssen's Cyclop.* XIII.; NOTHNAGEL, *Samml. klin. Vorträge* 103, trans. New. Syd. Soc. London 1877; PIERSON, *Ueb. Polyneuritis acuta, ibid.* 229; GEPPERT, *Multiple Neuritis, Charité-Annalen* 1883; STRÜMPELL, *Arch. f. Psych.* XIV. (*Neurolog. Centralb.* 1884); MÜLLER, *ibid.*; VIERORDT, *ibid.*; ROTH, *Neuritis dissem. acutissima, Corresp. f. Schweizer Aerzte* 1883; DUBOIS, *Multiple Neuritis, ibid.*; BAELZ, *Kakke oder Beriberi* Yokohama 1882, *Zeitschr. f. klin. Med.* IV. 1882; SCHEUBE, *Virch. Arch.* vol. 95, *D. Arch. f. klin. Med.* XXXI., XXXII., *Die japanische Kakke* Leipzig 1882; HIRSCH, *Handb. d. hist. geog. Path.* (2d edition), trans. by CREIGHTON (New Syd. Soc.) II. London 1885 (beriberi, with full references); CASPARI, *Zeitschr. f. klin. Med.* 1883; DÉJÉRINE, *Arch. de physiol.* 1884; WEBBER, *Archives of medicine* 1884; OPPENHEIM, *D. Arch. f. klin. Med.* XXXVI. 1885; BUZZARD, *Paralysis from peripheral neuritis* London 1886.

On neuritis in infective diseases:—BERNHARDT, *Arch. f. Psych.* IV.; JOFFROY, *loc. cit.*; NOTHNAGEL, *D. Arch. f. klin. Med.* IX. (1872); EISENLOHR, *Arch. f. Psych.* VI.; CORMACK, *Clinical Studies* London 1876; MURCHISON, *Continued fevers* London 1884; CHARCOT, *Diseases of the nervous system* II. London 1880; BUHL, *Zeitschr. f. Biol.* III.; OERTEL, *D. Arch. f. klin. Med.* VIII.; DÉJÉRINE, *Arch. d. physiol.* V. 1878; BUZZARD, *Lancet* 1, 1879, and *op. cit*; PITRES and VAILLARD, *Rev. de médecine* 1885; ROSS, *Diseases of the nervous system* II. London 1883 (with many references); P. KIDD, *Med. chir. Trans.* LXVI. 1883 (diphtherial paralysis).

On neuritis in herpes zoster see Art. 383; DUBLER, *Neuritis bei Herpes zoster* In. Diss. Basle 1884.

CHAPTER CIII.

TUMORS.

670. Most of the **tumors** which occur in the nerves and their ganglia are developed from connective tissue, and consist essentially of some modification of that tissue, the nerve-elements forming little or no part of their structure.

The fibrous hyperplasia usually starts from the perineurium of the nerves or nerve-bundles, but occasionally from the epineurium or endo-

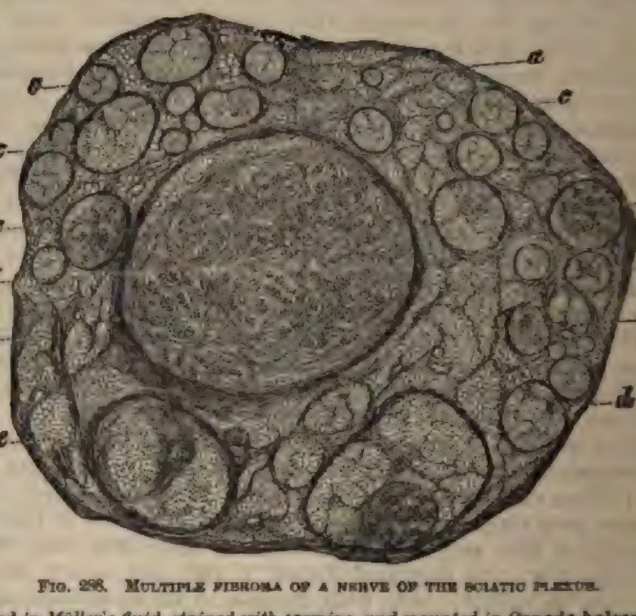

FIG. 288. MULTIPLE FIBROMA OF A NERVE OF THE SCIATIC PLEXUS.

(*Hardened in Müller's fluid, stained with carmine, and mounted in Canada balsam:* × 10.)

a, general perineurium
b, epineurium containing numerous fat-cells
c, nerve-bundle enclosed in a special perineurium
d, commencing fibroma in the endoneurium
e, more advanced fibroma within a nerve-bundle containing atrophied fibres
f, large fibroma-nodule within a bundle whose perineurium is thickened

neurium (Fig. 288 *d e f*). The nerves are embedded or pervaded by the new tissue, according to its starting-point, and by gradual compression become atrophied and break down. If there is any accompanying

nervous hyperplasia it probably takes place by the longitudinal subdivision and growth of pre-existing fibres: the new-formed fibres are at first naked, but some of them receive a medullary sheath in course of time.

The commonest neoplasm affecting the nerves is **fibroma** (Fig. 288): there are two forms—the soft and cellular, and the firm and fibrous. Tumors really deserving the name of **neuroma,** *i. e.* consisting essentially of new-formed nerve-fibres, are rare; and still rarer, if they exist at all, are tumors containing new-formed ganglion-cells, though these are described under the name of cellular or **ganglionic neuroma.**

Fibromata incorrectly described as neuromata are solitary or multiple, and in the latter case are congenital or at least appear soon after birth. Obviously the foundation of these structures is laid during fœtal life; sometimes their heredity can be demonstrated. They occur in nerve-trunks and on their finest twigs and branches, forming fusiform, nodular, or very elongated thickenings of the nerve or nerves. Sometimes a nerve is found thickened over its whole extent, with perhaps occasional fusiform swellings.

The spinal nerves are the most frequent seat of these growths, though they also occur on the cranial nerves. Sometimes all the nerves are simultaneously affected, even the finest branches showing thickenings and knotty swellings. Thus all the branches of the vagus in the lungs and stomach, or those of the sympathetic in the liver, have been described as covered with fibromata, but these cases are very rare. Not infrequently however we find the smaller cutaneous nerves beset with small round or flat usually soft tumors, some being buried in the skin, others protruding. These growths are known as **fibroma molluscum** (VON RECKLINGHAUSEN, Art. 399). The cutaneous nodules are often in great numbers and extend over the territory of a particular nerve or over the whole body; they are sometimes accompanied by neurofibromata of the internal organs. Sometimes too between the nodules extensive hyperplasia of the subcutaneous and cutaneous fibrous tissue takes place, and large soft masses and folds are thus produced and known as **pachydermatocele,** elephantiastic molluscum, elephantiasis mollis or neuromatous elephantiasis (Art. 399). The smallest growths may only be visible with a lens, the largest are sometimes the size of a kidney or larger.

The fusiform or nodose thickening of a nerve is often due to a single tumor; but a nerve-trunk sometimes includes several nodules in its cross-section, some lying in all or most of its bundles (Fig. 288). A central node will give rise to a fibrous tumor surrounded by nerve-bundles and a perineurium: when the fibroma starts in one of the outside bundles it at length appears as if seated on the nerve-trunk.

At times most of the nodes are confined to a single nerve. Other nodes, and these occasionally very large, consist of a plexus of many nerves united into a mass by hyperplastic fibrous tissue. The nerves are all

thickened, nodular, fusiform, convoluted, twisted, or otherwise distorted (Fig. 289), so that a coil of ravelled and varicose cords is formed, the whole being held together by fibrous tissue. Such a growth is described as a **plexiform neurofibroma.** According to P. BRUNS the cords contain numerous nerve-fibres, and it is therefore probable that new-formed nerve-fibres as well as fibrous tissue take part in its construction.

Of the other connective-tissue growths sarcoma, myxoma, and lipoma occur in connection with the nerves. The external forms they assume are similar to those of fibroma, but they are never multiple.

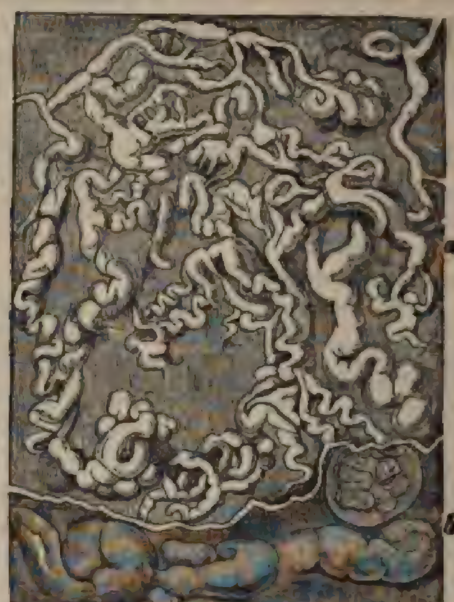

FIG. 289. PLEXIFORM NEUROFIBROMA OF THE SACRUM.

(*Natural size: from a drawing by P. BRUNS.*)

a, convoluted strands laid bare by dissection
b, as they appear covered with fibrous tissue

On neurofibroma:—VIRCHOW, *Krankhafte Geschwülste* III. (1863); HITCHCOCK, *Amer. Journ. med. sci.* 1862; CZERNY, *Arch. f. klin. Chir.* XVII. 1874; P. BRUNS, *Virch. Arch.* vol. 50; VON RECKLINGHAUSEN, *Ueb. mult. Fibrome d. Haut* Berlin 1882; KÖBNER, *Virch. Arch.* vol. 93; LAHMANN, *ibid.* vol. 101; NICAISE, *Internat. ency. of surgery* III. London 1883; PRUDDEN, *Amer. Journ. med. sci.* 1880 (with cases); COURVOISIER, *Die Neurome* Basle 1886 (with numerous references); CHAVASSE, *Med. chir. Trans.* LXIX. 1886. Tumors (fibroma, fibrosarcoma, neurofibroma) occur more frequently on the auditory than on other cranial nerves; see VIRCHOW, (*op. cit.*), and AXEL KEY (*Särskildt af Nordiskt med. Arkiv* XI. 1879).

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